Thromboprophylaxis for trauma patients (Review)

Barrera LM, Perel P, Ker K, Cirocchi R, Farinella E, Morales Uribe CH

This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2013, Issue 3

http://www.thecochranelibrary.com

TABLE OF CONTENTS

[Intervention Review]

Thromboprophylaxis for trauma patients

Luis M Barrera[1], Pablo Perel[2], Katharine Ker[2], Roberto Cirocchi[3], Eriberto Farinella[4], Carlos Hernando Morales Uribe[1]

[1]Department of General Surgery, Universidad de Antioquia, Medellin, Colombia. [2]Cochrane Injuries Group, London School of Hygiene & Tropical Medicine, London, UK. [3]Department of General Surgery, University of Perugia, Terni, Italy. [4]General and Colorectal Surgery, Lister Hospital - East and North Herts NHS Trust, Stevenage, UK

Contact address: Luis M Barrera, Department of General Surgery, Universidad de Antioquia, Street 67 N 53-108, Medellin, Colombia. luismbarrera@cable.net.co. bluis73@hotmail.com.

Editorial group: Cochrane Injuries Group.
Publication status and date: New, published in Issue 3, 2013.
Review content assessed as up-to-date: 30 April 2009.

Citation: Barrera LM, Perel P, Ker K, Cirocchi R, Farinella E, Morales Uribe CH. Thromboprophylaxis for trauma patients. *Cochrane Database of Systematic Reviews* 2013, Issue 3. Art. No.: CD008303. DOI: 10.1002/14651858.CD008303.pub2.

ABSTRACT

Background

Trauma is a leading causes of death and disability in young people. Venous thromboembolism (VTE) is a principal cause of death. Trauma patients are at high risk of deep vein thrombosis (DVT). The incidence varies according to the method used to measure the DVT and the location of the thrombosis. Due to prolonged rest and coagulation abnormalities, trauma patients are at increased risk of thrombus formation. Thromboprohylaxis, either mechanical or pharmacological, may decrease mortality and morbidity in trauma patients who survive beyond the first day in hospital, by decreasing the risk of VTE in this population.

A previous systematic review did not find evidence of effectiveness for either pharmacological or mechanical interventions. However, this systematic review was conducted 10 years ago and most of the included studies were of poor quality. Since then new trials have been conducted. Although current guidelines recommend the use of thromboprophylaxis in trauma patients, there has not been a comprehensive and updated systematic review since the one published.

Objectives

To assess the effects of thromboprophylaxis in trauma patients on mortality and incidence of deep vein thrombosis and pulmonary embolism. To compare the effects of different thromboprophylaxis interventions and their effects according to the type of trauma.

Search methods

We searched The Cochrane Injuries Group Specialised Register (searched April 30 2009), Cochrane Central Register of Controlled Trials 2009, issue 2 (*The Cochrane Library*), MEDLINE (Ovid) 1950 to April (week 3) 2009, EMBASE (Ovid) 1980 to (week 17) April 2009, PubMed (searched 29 April 2009), ISI Web of Science: Science Citation Index Expanded (SCI-EXPANDED) (1970 to April 2009), ISI Web of Science: Conference Proceedings Citation Index-Science (CPCI-S) (1990 to April 2009).

Selection criteria

Randomized controlled clinical trials involving people of any age with major trauma defined by one or more of the following criteria: physiological: penetrating or blunt trauma with more than two organs and unstable vital signs, anatomical: people with an Injury Severity Score (ISS) higher than 9, mechanism: people who are involved in a 'high energy' event with a risk for severe injury despite stable or normal vital signs. We excluded trials that only recruited outpatients, trials that recruited people with hip fractures only, or people with acute spinal injuries.

Data collection and analysis

Four authors, in pairs (LB and CM, EF and RC), independently examined the titles and the abstracts, extracted data, assessed the risk of bias of the trials and analysed the data. PP resolved any disagreement between the authors.

Main results

Sixteen studies were included (n=3005). Four trials compared the effect of any type (mechanical and/or pharmacological) of prophylaxis versus no prophylaxis. Prophylaxis reduced the risk of DVT in people with trauma (RR 0.52; 95% CI 0.32 to 0.84). Mechanical prophylaxis reduced the risk of DVT (RR = 0.43; 95% CI 0.25 to 0.73). Pharmacological prophylaxis was more effective than mechanical methods at reducing the risk of DVT (RR 0.48; 95% CI 0.25 to 0.95). LMWH appeared to reduce the risk of DVT compared to UH (RR 0.68; 95% CI 0.50 to 0.94). People who received both mechanical and pharmacological prophylaxis had a lower risk of DVT (RR 0.34; 95% CI 0.19 to 0.60)

Authors' conclusions

We did not find evidence that thromboprophylaxis reduces mortality or PE in any of the comparisons assessed. However, we found some evidence that thromboprophylaxis prevents DVT. Although the strength of the evidence was not high, taking into account existing information from other related conditions such as surgery, we recommend the use of any DVT prophylactic method for people with severe trauma.

PLAIN LANGUAGE SUMMARY

Preventing death from blood clots, the formation of blood clots and blood clots in the lungs in people who have had physical trauma

Thromboembolism (unwanted clotting of the blood) is a frequent complication in people who have experienced physical trauma and is also an important cause of death. The type of trauma, association with vascular injuries, and prolonged hospital bed rest are known risk factors for the development of deep vein thrombus (clot in veins of lower extremities) that can travel (embolize) to the lungs and cause death. Because of this it is usually recommended that people who have had major trauma are given mechanical or pharmacological treatments to prevent their blood forming unwanted blood clots. Mechanical interventions can include compression stockings, an air-filled plastic tube that presses around the leg, a metal blood clot filter placed inside a vein; pharmaceutical drugs include unfractionated heparin, low weight molecular heparin, anticoagulants (e.g. warfarin), antiplatelet drugs (e.g. aspirin) and others. Sixteen studies involving 3,005 people are included in this review. We did not find strong evidence that either mechanical or pharmacological interventions reduce death or clots travelling to the lungs, but we found some evidence that they can prevent clots from forming in the legs.

BACKGROUND

Description of the condition

Trauma is one of the leading causes of death and disability in young people (Evans 2003). Worldwide, about five million people die as a result of trauma every year (WHO 2008). For patients who reach hospital within one hour of trauma (called the 'golden hour'), blood loss and traumatic brain injury are the main causes of death (Sauaia 1995). For patients who survive beyond the first day, multiple organ failure, central nervous system (CNS) injury and venous thromboembolism (VTE) are the principal causes of death (Acosta 1998).

Trauma patients are at known risk of entering into a hypercoagulable state (intrinsic alterations in the nature of the blood itself). Mechanisms of hypercoagulability in the trauma setting include stasis, vessel wall dysfunction and alterations in clotting mechanisms (Virchow's triad). Injured patients are often immobilized after high-energy trauma. Being in a static position causes a reduction in venous blood returns and a decrease in the supply of oxygen and nutrients to endothelial cells. In addition, endothelial

damage caused by direct trauma to the vessels causes the exposition of tissue factor bearing cells. This initiates a procoagulant factor that amplifies the coagulant response. These tissue factor bearing cells move to the cell surface of the platelets, which produces a propagation of the signal through the accumulation of thrombin, activated cofactors and more platelets, inducing thrombosis (Hoffman 2001).

On the other hand, trauma patients experience a reduction of fibrinolytic pathways that seems to result from increased plasminogen activator inhibitor (PAI) 1. PAI 1 inhibits tissue plasminogen activator (tPA) and thus decreases the production of plasmin (Rogers 1995; Kelsey 2000). Coagulation abnormalities and the reduced ability to use the muscular pump of the calf in the injured patient can produce deep venous thrombosis (DVT) in the inferior and superior extremities (Spaniolas 2008). When the thrombus extends to the proximal segments, there is an increased risk of clot migration to the lungs and a fatal outcome (Geerts 2008).

Trauma patients are at high risk for DVT, with an incidence of 11.8% to 65% (Sevitt 1961; Geerts 1994; Velmahos 2000). The incidence varies according to the method used to measure the DVT and the location of the thrombosis. Incidence of thrombosis in the thigh (proximal DVT) is estimated at 18% (Geerts 1994). The incidence of pulmonary embolism (PE) is estimated between 1.5% and 20% (Shackford 1988; O'Malley 1990; Velmahos 2000). Many risk factors for DVT and PE in trauma patients have been identified such as spinal cord injury, lower extremity and pelvic fractures, need for surgical procedures, increasing age, femoral venous line insertion or surgical repair of venous injuries, prolonged immobility, long duration of hospital stay, severity of the trauma, and mechanism of injury (Geerts 1994; Knudson 1994; Frezza 1996; Velmahos 2000; Cipolle 2002; Rogers 2002; Meissner 2003).

Description of the intervention

Thromboprophylaxis describes any intervention used to prevent the development of VTE, and can be categorized into mechanical and pharmacological interventions.

External mechanical devices such as graded compression devices or intermittent pneumatic compression (IPC) have been shown to be effective in preventing DVT, but they cannot be used in patients with lower extremity trauma (Fisher 1995; Elliott 1999; Velmahos 2000). Internal mechanical devices are used to prevent the migration of thrombus from DVT to the lungs, thus preventing PE. One such device is the inferior vena cava filter (IVCF) which may be particularly useful in trauma patients because of the risk of ongoing bleeding at injured sites (McMurty 1999).

Pharmacological thromboprophylaxis was first described in the 1940s by Bauer 1944, and since then a number of interventions have been proposed. The anticoagulant effect of unfractionated heparin (UH) is initiated by the activation of antithrombin III (ATIII). The ATIII/heparin complex inactivates the thrombin factor IIa, and factors Xa, IXa, XIa and XIIa. However, UH is associated with a number of adverse events, such as thrombocytopenia. More recently, alternatives such as low molecular weight heparin (LMWH), a derivative of UH, have been proposed. LMWH acts in the same way as UH, but its low molecular weight fragments reduce the binding to other cells and proteins (and it also has a major affinity to factor Xa) (Hirsh 2004). These drugs have potential as effective prophylactic interventions for trauma, although there is concern due to the associated increased risk of bleeding (Geerts 1996; Haentjens 1996; Knudson 1996; Cohn 1999). Other methods of thromboprophylaxis, such as anticoagulants (warfarin) or antiplatelets (aspirin), seem less practical for use in critically ill patients, because of their delayed action and oral presentation. Pentassacharides (a new class of synthetic selective factor Xa inhibitor, with parenteral presentation which does not bind to platelets, other cells or proteins) have been studied as prophylaxis in surgical orthopedic patients and have been shown to be as effective as UH and LMWH (Nijkeuter 2004).

How the intervention might work

Due to prolonged rest and coagulation abnormalities, trauma patients are at increased risk of thrombus formation. Thromboprophylaxis, either mechanical or pharmacological, may decrease the mortality and morbidity in trauma patients who survive beyond the first day in hospital, by decreasing the risk of DVT and PE in this population. A previous Cochrane review focusing on high-risk patients indicated that combined methods (pharmacologic and mechanical interventions) decreased the incidence of DVT (Kakkos 2008). However, this systematic review did not examine the effects in the subgroup of trauma patients.

Why it is important to do this review

Trauma patients are at an increased risk of VTE, and thromboprophylaxis has the potential to be effective in this population. However, trauma patients are at an increased risk of bleeding, which is one of the adverse events associated with pharmacological interventions. For some trauma patients with injured extremities, the use of mechanical interventions (e.g. external mechanical compression) is not feasible. A previous systematic review (Velmahos 2000) did not find evidence of effectiveness for either pharmacological or mechanical interventions. However, this systematic review was conducted 10 years ago and most of the included studies were of poor quality. Since then new trials have been conducted. Although current guidelines (Rogers 2002; Geerts 2008) recommend the use of thromboprophylaxis in trauma patients, there has not been a comprehensive and updated systematic review since the one published by Velmahos et al. Furthermore, there are still uncertainties about the relative benefit of interventions for different subgroups of trauma patients. Therefore it is necessary to con-

duct a systematic review to establish whether the effect of different thromboprophylaxis interventions varies according to the type of trauma, location of the trauma, severity of trauma and type of management (surgical or medical management).

OBJECTIVES

To assess the effects of thromboprophylaxis in trauma patients on mortality and incidence of DVT and PE.

To compare the effects of different thromboprophylaxis interventions and their effects according to the type of trauma.

METHODS

Criteria for considering studies for this review

Types of studies

Randomized controlled clinical trials.

Types of participants

People of any age with major trauma defined by one or more of the following criteria;

- physiological: penetrating or blunt trauma with more than two organs and unstable vital signs,
- anatomical: patients with an Injury Severity Score (ISS) higher than 9,
- mechanism: patients who are involved in a 'high energy' event with a risk for severe injury despite stable or normal vital signs.

We excluded trials that only recruited outpatients, trials than recruited patients with hip fractures only, or patients with only acute spinal injuries.

Types of interventions

We included trials investigating any of the following interventions;

1. Unfractionated heparin (UH),
2. Low weight molecular heparin (LWMH),
3. Mechanical methods: graded compression stocking, and sequential compression devices,
4. Oral anticoagulants (e.g. warfarin),
5. Antiplatelet drugs (e.g. aspirin),
6. Pentassacharides,
7. Pulmonary embolism prophylaxis (e.g. inferior vena cava filter (IVCF)).

We compared the effects of any intervention with placebo, and any two interventions (e.g. LMWH versus UH) or combination of interventions (UH plus mechanical methods versus UH).

Types of outcome measures

Primary outcomes

The primary outcome was mortality.

Secondary outcomes

The secondary outcomes were the incidence of DVT, PE and adverse events, such as:

- bleeding (major and minor);
- whether the adverse event (bleeding of the injured site, intracranial bleeding, gastrointestinal bleeding, epistaxis, etc.) required transfusion or any procedure to control it;
- and other adverse events as defined by the trial authors.

Search methods for identification of studies

We did not restrict searches by date, language or publication status.

Electronic searches

We searched the following electronic databases:

- Cochrane Injuries Group's Specialised Register (searched April 30 2009);
- Cochrane Central Register of Controlled Trials 2009, issue 2 (*The Cochrane Library*);
- MEDLINE (Ovid) 1950 to April (week 3) 2009;
- EMBASE (Ovid) 1980 to (week 17) April 2009;
- PubMed [http://www.ncbi.nlm.nih.gov/sites/entrez] (searched 29 April 2009);
- ISI Web of Science: Science Citation Index Expanded (SCI-EXPANDED) (1970 to April 2009);
- ISI Web of Science: Conference Proceedings Citation Index-Science (CPCI-S) (1990 to April 2009).

Search strategies are listed in full in Appendix 1.

Searching other resources

We searched the bibliographies of all included studies and other relevant papers for further potentially eligible trials. We searched the Internet using the Google (www.google.com) search engine with selected terms from the strategy to identify any further unpublished or grey literature.

Data collection and analysis

The Injuries Group Trials Search Co-ordinator ran the electronic database searches, collated the search results, removed duplicates then sent the remaining records to the authors for screening

Selection of studies

Four authors, in pairs (LB and CM, EF and RC), independently examined titles, abstracts, and keywords of citations from electronic databases for eligibility. We obtained the full texts of all potentially relevant records and two authors (EF and CM) independently assessed whether each met the pre-defined inclusion criteria. We resolved any disagreement through discussion with a third author (PP).

Data extraction and management

Four authors, in pairs (LB and CM, EF and RC) extracted data independently, using a standardized data extraction form. LB entered the extracted information into Review Manager (RevMan 2008) for analysis. We extracted data on the following:

1. General Information: title, authors, source of publication, country, published or not, language and year of publication.
2. Trial characteristics: study design and information that meets the Cochrane Collaboration's tool for assessing risk of bias.
3. Participants: sample size, inclusion criteria, exclusion criteria, location of trauma (brain, chest, abdomen, pelvis, extremity, polytrauma), severity of trauma (ISS, RTS, or according to the scale used by the trialists), type of injury (blunt or penetrating), and type of surgical procedure (non-operative or surgical management).
4. Intervention: type and dose of thromboprophylaxis used, type and dose of control or placebo used.
5. Outcomes: incidence of mortality, incidence of DVT (symptomatic or asymptomatic) and diagnostic test used, incidence of PE and diagnostic test used. Incidence of adverse events as follows: any bleeding, major bleeding defined as use of transfusion or any procedure to control bleeding (bleeding from the injured site, gastrointestinal bleeding, brain bleeding, epistaxis, etc.) and minor bleeding. Other outcomes recorded by the authors.
6. Results: number of patients in each group, missing patients.
7. Subgroup characteristics: number of patients by localization of trauma, by severity, by type (blunt or penetrating), by type of management (surgical or non-surgical).
8. Other information: funding source.

Assessment of risk of bias in included studies

Four authors in pairs (LB and CM, EF and RC) assessed the risk of bias of each included trial using the Cochrane Collaboration's tool for assessing risk of bias presented in Higgins 2008. We assessed the following domains: sequence generation; allocation concealment; blinding; incomplete outcome data; and selective outcome reporting. We completed risk of bias tables for each trial, incorporating a description of the trial's performance against each domain and our overall judgment of the risk of bias for each entry as follows: 'Yes' for low risk of bias; 'No' for high risk of bias, or 'Unclear'. We resolved disagreements by consulting a third author (PP).

Measures of treatment effect

For dichotomous data we calculated risk ratios (RR) and 95% confidence intervals (CIs). We also calculated number needed to treat (NNT) and number needed to harm (NNH).

For continuous data we calculated the mean difference (MD) and 95% CIs when the same scale was used in a similar manner across studies. If results for continuous outcomes were reported using different scales or different versions of the same scale, we calculated the standardised mean difference (SMD) and 95% CIs.

Dealing with missing data

We did not contact the trial authors for missing information.

Assessment of heterogeneity

We examined trial characteristics in terms of participants, interventions and outcomes for evidence of clinical heterogeneity. We examined statistical heterogeneity by both the I^2 statistic and Chi ^{2} test. The I^2 statistic describes the percentage of total variation across studies due to heterogeneity rather than chance. A value of 0% indicates no observed heterogeneity, and larger values show increasing heterogeneity; substantial heterogeneity is considered to exist when I^2 is larger than 50%. For the Chi^2 test, we used a p value of less than 0.10 to indicate the presence of statistically significant heterogeneity.

Assessment of reporting biases

We planned to investigate the presence of reporting (publication) bias using funnel plots, however there were too few included trials contributing data to each outcome to enable meaningful analysis.

Data synthesis

We judged that the trials were sufficiently homogenous, both clinically and statistically, to pool the outcome data. Dichotomous data were pooled using the Mantel-Haenszel fixed-effect method and continuous data were pooled using the fixed-effect inverse-variance method.

Because different effects were expected according to the intervention, we performed data synthesis separately for each type (e.g. UH, LWMH or mechanical devices).

Subgroup analysis and investigation of heterogeneity

There were insufficient data to perform the following planned subgroup analyses:

- type of trauma (blunt, penetrating);
- location of the trauma (brain, chest, abdominal, pelvis, extremity or polytrauma);
- severity of trauma defined with ISS or other similar scores;
- management (surgical or medical management);
- diagnostic method.

Sensitivity analysis

We performed a sensitivity analysis to investigate whether the results were robust. We examined the effect of excluding certain studies according to their risk of bias. We reported the data synthesis for all the included studies and repeated the calculations after excluding studies judged as having a high risk of bias for allocation concealment. We also examined the effect of using a different effect measure (odds ratio) for the dichotomous outcomes.

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies.

Results of the search

The combined search strategy identified 2858 citations, of which 38 were judged to be potentially eligible based on title or abstract, or both, and the full texts were obtained. After a full text review, 16 trials were judged to be eligible and were included in the review, one was reported as an abstract.

Included studies

We included 3005 people of any age who had major trauma. 1898 people had blunt trauma and 225 people had penetrating trauma. Four trials did not report the injury mechanism (Fuchs 2005; Ginzburg 2003; Knudson 1996; Yanar 2007). Most of the studies reported the ISS. The average of the ISS reported by the trials varies between 13 and 30. Five studies did not report the ISS value. Six studies reported a specific management. 816 with operative treatment and 173 with non operative treatment.

The Knudson 1994 All groups study was divided in four groups: Knudson 1994 All groups, Knudson 1994 group I (UH vs SCD vs Placebo), Knudson 1994 group II (UH vs Placebo) and Knudson 1994 group III (SCD vs Placebo).

Four trials compared a method of prophylaxis with no prophylaxis (Dennis 1993; Fisher 1995; Knudson 1994 All groups; Velmahos 2005).

Two trials compared pharmacological methods (LMWH with UH) (Cohn 1999; Geerts 1996).

Three trials compared mechanical methods (thigh calf sequential compression device with a foot-calf pump) (Anglen 1998; Elliot 1999; Stannard 2001).

Five trials compared pharmacological with mechanical methods, of which three compared LMWH with Intermittent Pneumatic Compression (IPC) devices (Ginzburg 2003; Kurtoglu 2004; Yanar 2007) and two compared UH with Sequential Compression Devices (SCD) (Knudson 1992; Knudson 1994 group I).

Four trials compared a combination of pharmacological and mechanical interventions. One trial allocated patients to three groups to compare IPC, IPC plus LMWH and LMWH alone (Yanar 2007). The other three trials compared pharmacological plus mechanical methods with pharmacological prophylactics (Fuchs 2005; Stannard 2006; Yanar 2007).

All 16 trials used doppler ultrasound (Duplex) to diagnose DVT. The diagnosis was confirmed with venography in three trials (Geerts 1996; Fuchs 2005; Fisher 1995), and by Duplex and MRI venography in one trial (Stannard 2001).

Sixteen trials presented data on pulmonary embolism. PE was diagnosed clinically in two trials (Anglen 1998; Fuchs 2005); by a V/Q scan and pulmonary angiography in five trials (Knudson 1992; Knudson 1994 All groups; Knudson 1996; Geerts 1996; Cohn 1999); by CT scan angiography on clinically suspected cases in two trials (Kurtoglu 2004; Yanar 2007); by clinical suspicion and autopsy in one trial (Elliot 1999); by angiography and autopsy in two trials (Fisher 1995; Dennis 1993); by used ventilation/perfusion scan (V/Q scan), angiography and CT scan angiography in one trial (Ginzburg 2003); and by MRI angiography in one trial (Stannard 2006). The method used in the remaining two trials was not described (Velmahos 2005; Stannard 2001).

Further details of the individual trials are presented in the Characteristics of included studies table.

Excluded studies

Of the trials excluded from our review three were not randomised (Greenfiel 1997; Holzheimer 2004; Reilmann 1986), two included only outpatients or elective surgery patients (Haas 2003; Wolf 1992), one involved hip fracture surgery patients (Breyer 1986) and one did not measure any outcomes of interest to this review (Murakami 2003).

Details are presented in the Characteristics of excluded studies.

Risk of bias in included studies

Allocation

Eleven of the 16 studies had a low risk in the sequence generation of the treatment groups, three of them had high risk of bias and two were unclear.
In half of the studies included the allocation concealment was unclear, four of the 16 had low risk in the allocation and the other four studies had high risk of bias.

Blinding

Blinding was well conducted in seven of the 16 studies, in five there was a high risk of bias and in four the data were insufficient to establish the quality of blinding.

Incomplete outcome data

Six studies performed an intention to treat analysis, in nine there was a high risk bias because outcome data were analysed in an incomplete fashion, and just one of them did not allow us to establish the risk.

Selective reporting

We were unable to obtain the protocols for any of the trials, therefore the reporting bias was unclear for all 16 trials.

Effects of interventions

All the collected material allowed us to perform 7 comparisons, we made four comparisons as a sensitivity analysis. As established in the protocol we compared any method of prophylaxis versus no prophylaxis, between prophylaxis methods and combinations of them. The most important are highlighted in this text section. The detailed analysis can be seen in the Data and analyses section.

Prophylaxis versus no prophylaxis

Four trials involving 997 people compared the effect of any type (mechanical and/or pharmacological) of prophylaxis versus no prophylaxis. Prophylaxis reduced the risk of DVT in trauma patients (RR 0.52; 95% CI 0.32 to 0.84). There was no evidence of statistical heterogeneity between trials (I^2=12%; Chi^2 P=0.333). There was no evidence for an effect on PE (RR 0.65; 95% CI 0.29 to 1.43) or mortality (RR 0.59; 95% CI 0.20 to 1.70).
Three trials reported the effect on bleeding, no events were observed in any trial.

Mechanical prophylaxis versus no prophylaxis

Six trials involving 811 people compared the effect of mechanical prophylaxis with no prophylaxis.
Mechanical prophylaxis reduced the risk of DVT (RR 0.55; 95% CI 0.34 to 0.90). There was no evidence of statistical heterogeneity between trials (I^2 = 22%, Chi^2 P=0.28). There was no evidence that mechanical prophylaxis reduced the risk of PE (RR 0.77; 95% CI 0.36 to 1.66) or death (RR 0.74; 95% CI 0.27 to 2.04).
Four trials (507 patients) reported the effect on bleeding, no events were observed in any trial.

Pharmacological prophylaxis versus mechanical prophylaxis

Six trials involving 1033 people compared pharmacological prophylaxis with mechanical prophylaxis.
Pharmacological prophylaxis was more effective than mechanical methods at reducing the risk of DVT (RR 0.48; 95% CI 0.25 to 0.95). There was no evidence of heterogeneity between trials (I^2=0%, Chi^2 P=0.56). There was no evidence for a difference in effect on the risk of PE (RR 0.94; 95% CI 0.36 to 2.42) or death (RR 1.50; 95% CI 0.44 to 5.16).
Five of the trials (953 patients) reported bleeding outcome data. Pharmacological prophylaxis increased the risk of bleeding (RR 2.04; 95% CI 1.08 to 3.86) compared to mechanical methods. There was no evidence of heterogeneity (I^2=0%, Chi^2 P=0.53).
Three trials (764 patients) distinguished between major and minor bleeding. There was no evidence for a difference in effect on the risk of major bleeding (RR 1.03; 95% CI 0.26 to 4.06). However, pharmacological prophylaxis increased the risk of minor bleeding (RR 2.37; 95% CI 1.13 to 4.98). There was no evidence for heterogeneity between trials (I^2=0%; Chi^2 P=0.64).

Low Molecular Weight Heparin versus Unfractionated Heparin

Two trials involving 331 patients compared low molecular weight heparin (LMWH) with unfractionated heparin (UH). LMWH appeared to reduce the risk of DVT compared to UH (RR 0.68; 95% CI 0.50 to 0.94). There was no evidence for heterogeneity between trials (I^2 = 0%, Chi^2 P=0.46).
There was no statistically significant difference in the risk of PE between the two groups (RR 3.16; 95% CI 0.13 to 76.91) and there were no deaths reported in either trial.
There was no statistically significant difference in the risk of bleeding between LMWH and UH (RR 1.63; 95% CI 0.63 to 4.22).

Mechanical plus pharmacological prophylaxis versus Pharmacological prophylaxis

Three trials involving 507 patients compared mechanical prophylaxis plus pharmacological prophylaxis with pharmacological prophylaxis alone. Patients who received both mechanical and pharmacological prophylaxis had a lower risk of DVT (RR 0.34; 95% CI 0.19 to 0.60). However, there was evidence for statistical heterogeneity between trials (I^2= 69%, Chi^2 P=0.04).

There was no evidence for a difference in effect on the risk of PE (RR 0.32; 95% CI 0.05 to 2.01) or death (RR 0.50; 95% CI 0.05 to 5.30).
One trial assessed the effect on bleeding and found no difference in the risk of bleeding between the two groups (RR 0.99; 95% CI 0.56 to 1.78).

Other comparisons

One study compared mechanical plus pharmacological prophylaxis versus mechanical prophylaxis (Yanar 2007) and did not find difference. Also three trials compared thigh-calf versus calf-foot methods (Anglen 1998; Elliot 1999; Stannard 2001) did not find either statistical difference.

Sensitivity Analyses

The sensitivity analysis included only the studies that were considered at low risk of bias for allocation concealment. We made four comparisons of the results, which showed a statistically significant difference.
The comparisons of prophylaxis vs no prophylaxis and mechanical methods vs no prophylaxis, could include only one study (Fisher 1995). It showed a tendency to be superior for prophylaxis, but without reaching a statistically significant difference (RR 0.35; 95% CI 0.11 to 1.10).
When we compare LMWH vs UH, we could include just one study (Geerts 1996) which showed strong evidence that LMWH was superior for prevention of DVT (RR 0.57; 95% CI 0.34 to 0.94).
When we compare mechanical with pharmacological prophylaxis we also could include just one study (Ginzburg 2003) but did not show any significant difference (RR 0.17; 95% CI 0.02 to 1.41).

DISCUSSION

Summary of main results

This systematic review gathers all the available evidence from all randomised controlled trials which compare the use of pharmacological and mechanical thromboprophylaxis in patients with severe trauma. We excluded trials that only recruited outpatients, patients presenting only with hip fractures, acute spinal injuries and low energy trauma.
Among trauma patients who did not receive any prophylaxis we found that deep venous thrombosis (DVT) incidence was 8.72% (37/424) diagnosed by Dupplex. The incidence of pulmonary embolism (PE) was 3.3% (14/424) for PE diagnosed by VQ scan or angiography or autopsy (Dennis 1993; Fisher 1995; Knudson 1994 All groups; Velmahos 2005).
We did not find evidence that thromboprophylaxis reduces the primary outcome mortality or the secondary outcome PE for any of the comparisons assessed.
However, we found some evidence of effective interventions for the prevention of the secondary outcome DVT. Prophylaxis was more effective than no prophylaxis, pharmacological prophylaxis than mechanical prophylaxis, and LMWH than UH. However, these results were based on a few small trials with relatively few events and poor methodology quality. We also found some evidence that patients who received pharmacological thromboprophylaxis have a higher risk of minor bleeding compared to patients who received mechanical therapy. At the moment there is no RCT published for major trauma with dabigatran or rivaroxiban.
Although the strength of the evidence found in this review was not strong our findings are similar to previous reviews conducted in different but related conditions (Surgical non traumatized, cancer, hip fractures) (Wille-Jørgensen 2008; Bani-Hani 2011; Handoll 2008). The present review strengthens the clinical practice guidelines recommendations from Eastern Association for the Surgery of Trauma (Rogers 2002) and American College of Chest Physicians (Kahn 2012; Geerts 2008), providing further evidence for thromboprophylaxis in patients with severe trauma.

Overall completeness and applicability of evidence

We did not find enough studies to allow any comparison between pharmacological prophylaxis against placebo. There are also not enough studies which evaluate specific pharmacological interventions (UW or LMWH) vs specific mechanical therapies (SCD or AVI).

Quality of the evidence

The quality of evidence was low as only one of the four studies included for the main comparison (prophylaxis versus no prophylaxis) had low risk of selection bias as judged by the allocation concealment process. Also the external validity could be threatened because of sponsorship by mechanical devices manufacturers (Velmahos 2005).

Potential biases in the review process

Potential biases in the review process are mainly defined by an impossibility to analyse a study due to an abstract inclusion in the meta-analysis (Yanar 2007). We tried to minimize selection bias by working, collecting and analysing all studies in pairs (LB-CM and EF-RC). All differences where resolved by consensus and also through the input of PP.

Agreements and disagreements with other studies or reviews

Previous meta-analyses (Velmahos 2000) have shown no evidence that low-dose unfractionated heparin, mechanical prophylaxis, or low-molecular weight heparin are more effective than no prophylaxis or among each other. In addition, unlike ours, this systematic review included observational studies which provide less reliable evidence of effectiveness for medical interventions.

A recent systematic review (Smith 2011) with severe skeletal trauma as its main inclusion criteria suggested that low molecular weight heparin (LMWH) may be superior to low dose heparin (LDH), and that LMWH should be used in addition to mechanical prophylaxis measures in patients following major skeletal trauma for the prevention of thromboembolic events, this findings do not differ from ours. The analysed studies were included in this meta-analysis, the difference between these systematic reviews were that they just include major skeletal trauma.

Bleeding was not analysed as an outcome in previous meta-analysis and not all of the trials considered bleeding as an outcome.

AUTHORS' CONCLUSIONS

Implications for practice

Although the strength of the evidence included in this review was not high, taking into account existing information from other related conditions such as surgery, we believe that the use thromboprophylaxis for preventing DVT in severe trauma patients is recommended.

Implications for research

Adequately powered trials should be conducted to compare different thromboprophylaxis strategies. Also we would recommend that future RCTs should have a more uniform and defined method of diagnosing both DVT and PE so as to measure the true effect thromboprophylaxis.

In addition to mortality, DVT and PE, future trials should assess the following outcomes which have important clinical implications:

1. Adverse events of pharmacological prophylaxis such as bleeding.

2. Post-discharge consequences of DVT in postraumatic patients including postphlebitic syndrome, chronic DVT or chronic PE.

ACKNOWLEDGEMENTS

We thank Karen Blackhall for designing and performing the bibliographic database searches.

REFERENCES

References to studies included in this review

Anglen 1998 *{published data only}*

Anglen JO, Bagby C, George R. A randomised comparison of sequential-gradient calf compression with intermittent plantar compression for prevention of venous thrombosis in orthopedic trauma patients: preliminary results. *American journal of orthopedics* 1998;**27**(1):53–8.

Cohn 1999 *{published data only}*

Cohn SM, Moller BA, Feinstein, AJ, Burns GA, Ginzburg E, Hammers LW. Prospective trial of low-molecular-weight heparin versus unfractionated heparin in moderately injured patients. *Vascular Surgery* 1999;**33**(2):219–23.

Dennis 1993 *{published data only}*

Dennis JW, Menawat S, Von Thron J, Fallon Jr WF, Vinsant GO, Laneve LM, et al.Efficacy of deep venous thrombosis prophylaxis in trauma patients and identification of high-risk groups. *The Journal of Trauma-injury and Critical Care* 1993;**35**(1):132–9.

Elliot 1999 *{published data only}*

Elliott CG, Dudney TM, Egger M, Orme JF, Clemmer TP, Horn SD, et al.Calf-thigh sequential pneumatic compression compared with plantar venous pneumatic compression to prevent deep-vein thrombosis after non-lower extremity trauma. *The Journal of Trauma-injury and Critical Care* 1999;**47**(1):25–32.

Fisher 1995 *{published data only}*

* Fisher CG, Blachut PA, Salvian AJ, Meek RN, O'Brien PJ. Effectiveness of pneumatic leg compression devices for the prevention of thromboembolic disease in orthopaedic trauma patients: a prospective, randomised study of compression alone versus no prophylaxis. *Journal of orthopaedic trauma* 1995;**9**(1):1–7.

Fisher CG, Blachut PA, Salvian AJ, Meek RN, O'Brien PJ. Effectiveness of pneumatic leg compression devices for the prevention of thromboembolic disease in orthopaedic trauma patients [Abstract]. *Journal of Bone and Joint Surgery - British Volume* 1991;**73 Suppl 1**:49–50.

Fuchs 2005 *{published data only}*

Fuchs S, Heyse T, Rudofsky G, Gosheger G, Chylarecki C. Continuous passive motion in the prevention of deep-vein thrombosis: a randomised comparison in trauma patients. *The Journal of bone and joint surgery. British volume.* 2005; **87**(8):1117–22.

Geerts 1996 *{published data only}*
Geerts WH, Jay RM, Code KI, Chen E, Szalai JP, Saibil EA, Hamilton PA. A comparison of low-dose heparin with low-molecular-weight heparin as prophylaxis against venous thromboembolism after major trauma. *The New England journal of medicine* 1996;**335**(10):701–7.

Ginzburg 2003 *{published data only}*
Ginzburg E, Cohn SM, Lopez J, Jackowski J, Brown M, Hameed SM, Miami Deep Vein Thrombosis Study Group. Randomized clinical trial of intermittent pneumatic compression and low molecular weight heparin in trauma. *British Journal of Surgery* 2003;**90**(11):1338–44.

Knudson 1992 *{published data only}*
Knudson MM, Collins JA, Goodman SB, McCrory DW. Thromboembolism following multiple trauma. *The Journal of Trauma-injury and Critical Care* 1992;**32**:2–11.

Knudson 1994 All groups *{published data only}*
Knudson MM, Lewis FR, Clinton A, Atkinson K, Megerman J. Prevention of venous thromboembolism in trauma patients. *The Journal of Trauma-injury and Critical Care* 1994;**37**(3):480–7.

Knudson 1994 group I *{published data only}*
Knudson MM, Lewis FR, Clinton A, Atkinson K, Megerman J. Prevention of venous thromboembolism in trauma patients. *The Journal of Trauma-injury and Critical Care* 1994;**37**(3):480–7.

Knudson 1994 group II *{published data only}*
Knudson MM, Lewis FR, Clinton A, Atkinson K, Megerman J. Prevention of venous thromboembolism in trauma patients. *The Journal of Trauma-injury and Critical Care* 1994;**37**(3):480–7.

Knudson 1994 group III *{published data only}*
Knudson MM, Lewis FR, Clinton A, Atkinson K, Megerman J. Prevention of venous thromboembolism in trauma patients. *The Journal of Trauma-injury and Critical Care* 1994;**37**(3):480–7.

Knudson 1996 *{published data only}*
Knudson MM, Morabito D, Paiement GD, Shackleford S. Use of low molecular weight heparin in preventing thromboembolism in trauma patients.. *Journal of Trauma-Injury Infection and Critical Care* 1996;**41**(3):446–59.

Kurtoglu 2004 *{published data only}*
Kurtoglu M, Yanar H, Bilsel Y, Guloglu R, Kizilirmak S, Buyukkurt D, Granit V. Venous thromboembolism prophylaxis after head and spinal trauma: intermittent pneumatic compression devices versus low molecular weight heparin. *World journal of surgery* 2004;**28**(8):807–11.

Stannard 2001 *{published data only}*
Stannard JP, Riley RS, McClenney MD, Lopez Ben RR, Volgas DA, Alonso JE. Mechanical prophylaxis against deep-vein thrombosis after pelvic and acetabular fractures.. *Journal of Bone and Joint Surgery - American Volume* 2001; **83 A**(7):1047–51.

Stannard 2006 *{published data only}*
Stannard JP, Lopez-Ben RR, Volgas DA, Anderson ER, Busbee M, Karr DK, McGwin GR, Alonso JE. The Journal of bone and joint surgery. American volume. *Prophylaxis against deep-vein thrombosis following trauma: a prospective, randomised comparison of mechanical and pharmacologic prophylaxis* 2006;**88**(2):261–6.

Velmahos 2005 *{published data only}*
Velmahos GC, Petrone P, Chan LS, Hanks SE, Brown CV, Demetriades D. Electrostimulation for the prevention of deep venous thrombosis in patients with major trauma: a prospective randomised study. *Surgery.* 2005;**137**(5): 493–8.

Yanar 2007 *{published data only}*
Yanar H, Kurtoglu M, Taviloglu K, Guloglu R, Ertekin C. Is intermittent pneumatic compression make low molecular weight heparin more efficient in the prophylaxis of venous thromboembolism in trauma patients. *European Journal of Trauma and Emergency Surgery* 2007;**33**(3 Suppl 2):79–80.

References to studies excluded from this review

Breyer 1986 *{published data only}*
Breyer HG, Al-Therib J, Bacher P, Werner B. Thrombosis prophylaxis with low molecular weight heparin in trauma surgery [Abstract]. *Thrombosis Research Supplement* 1986; **VI**:84.

Greenfiel 1997 *{published data only}*
Greenfield LJ, Proctor MC, Rodriguez JL, Luchette FA, Cipolle MD, Cho J. Posttrauma thromboembolism prophylaxis. *The Journal of Trauma-injury and Critical Care* 1997;**42**(1):100–3.

Haas 2003 *{published data only}*
Haas S, Lassen MR, Wolf H, Brom J, Weidinger G, Fareed J. Prevention of venous thromboembolism in orthopedic trauma patients receiving heparin thromboprophylaxis - a substudy analysis of autopsy-confirmed fatal pulmonary embolism. *Journal of Thrombosis & Haemostasis* 2003;**1** (Suppl 1):Abstract no: P1442.

Holzheimer 2004 *{published data only}*
Holzheimer RG. Prophylaxis of thrombosis with low molecular weight heparin. *European Journal of Medical Research* 2004;**9**:150–70.

Murakami 2003 *{published data only}*
Murakami M, McDill TL, Cindrick-Pounds L, Loran DB, Woodside KJ, Mileski WJ, et al.Deep venous thrombosis prophylaxis in trauma: improved compliance with a novel miniaturized pneumatic compression device. *Journal of vascular surgery* 2003;**38**(5):923–7.

Reilmann 1986 *{published data only}*
Reilmann H, Creutzig H, Tscherne H, Reilmann L. Langenbecks Archiv fur Chirurgie. *Medicamental prophylaxis of thromboembolic complications with heparin and dihydroergotamine in trauma surgery* 1986;**369**:753.

Wolf 1992 *{published data only}*
Wolf H, Kujath P, Spannagel U. Prevention of Thromboembolic Complications in Traumatized Patients - a Comparison Between Low-Molecular-Weight Heparin and Low-Dose Heparin. *Perfusion* 1992;**5**(7):210.

Additional references

Acosta 1998

Acosta JA, Yang JC, Winchell RJ, Simons RK, Fortlage DL, Hollingsworth-Fridlund P, et al.Lethal injuries and time to death in a level I trauma center. *Journal of the American College of Surgeons* 1998;**186**:528–33.

Bani-Hani 2011

Bani-Hani M, Titi MA, Jaradat I, Al-Khaffaf H. Interventions for preventing venous thromboembolism following abdominal aortic surgery. *Cochrane Database of Systematic Reviews* 2011, Issue 3.

Bauer 1944

Bauer G. Thrombosis following leg injuries. *Acta Chirurgica Scandinavica* 1944;**90**:229–48.

Cipolle 2002

Cipolle MD, Wojcik R, Seislove E, Wasser TE, Pasquale MD. The role of surveillance duplex scanning in preventing venous thromboembolism in trauma patients. *Journal of Trauma-Injury Infection & Critical Care* 2002;**52**:453–62.

Cohn 1999

Cohn SM, Moller BA, Feinstein AJ, Burns GA, Ginzburg E, Hammers LW. Prospective trial of low-molecular-weight heparin versus unfractionated heparin in moderately injured patients. *Vascular and Endovascular Surgery* 1999;**33**: 219–23.

Elliott 1999

Elliott CG, Dudney TM, Egger M, Orme JF, Clemmer TP, Horn SD, et al.Calf-thigh sequential pneumatic compression compared with plantar venous pneumatic compression to prevent deep-vein thrombosis after non-lower extremity trauma. *Journal of Trauma-Injury Infection & Critical Care* 1999;**47**:25–32.

Evans 2003

Evans SA, Airey MC, Chell SM, Connelly JB, Rigby AS, Tennant A. Disability in young adults following major trauma: 5 year follow up of survivors. *BioMed Central Public Health* 2003;**3**:8.

Fisher 1995

Fisher CG, Blachut PA, Salvian AJ, Meek RN, O'Brien PJ. Effectiveness of leg compression devices for the prevention of thromboembolic disease in orthopaedic trauma patients: a prospective, randomised study of compression alone versus no prophylaxis. *Journal of Orthopedics Trauma* 1995;**9**:1–7.

Frezza 1996

Frezza EE, Siram SM, van Thiel DH, Mezghebe MH. Venous thromboembolism after penetrating chest trauma is not a cause of early death. *Journal of Cardiovascular Surgery* 1996;**37**:521–4.

Geerts 1994

Geerts WH, Code KI, Jay RM, Chen RE, Szalai JP. A prospective study of venous thromboembolism after major trauma. *The New England Journal of Medicine* 1994;**331**: 1601–6.

Geerts 1996

Geerts WH, Jay RM, Code KI, Chen E, Szalai JP, Saibil EA, et al.A comparison of low-dose heparin with low-molecular-weight heparin as prophylaxis against venous thromboembolism after major trauma. *The New England Journal of Medicine* 1996;**335**:701–7.

Geerts 2008

Geerts WH, Bergqvist D, Pineo GF, Heit JA, Samama CM, Lassen MR, et al.Prevention of venous thromboembolism: American college of chest physicians evidence-based clinical practice guidelines (8th edition). *Chest* 2008;**133**(6 Suppl): 381–453.

Haentjens 1996

Haentjens P. Thromboembolic prophylaxis in orthopaedic trauma patients: a comparison between a fixed dose and an individually adjusted dose of a low molecular weight heparin (nadroparin calcium). *Injury* 1996;**27**:385–90.

Handoll 2008

Handoll HHG, Farrar MJ, McBirnie J, Tytherleigh-Strong GM, Milne AA, Gillespie WJ. Heparin, low molecular weight heparin and physical methods for preventing deep vein thrombosis and pulmonary embolism following surgery for hip fractures. *Cochrane Database of Systematic Reviews* 2008, Issue 4. [DOI: 10.1002/14651858.CD000305]

Higgins 2008

Higgins JPT, Green S (editors). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.0.1 [updated September 2008]. The Cochrane Collaboration, 2008. Available from www.cochrane-handbook.org.

Hirsh 2004

Hirsh J, Raschke R. Heparin and Low-Molecular-Weight Heparin. The Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. *Chest* 2004; **126**(Supplement):188–203.

Hoffman 2001

Hoffman M, Monroe D. A cell-based model of haemostasis. *Thrombosis and Haemostasis* 2001;**85**:958–65.

Kahn 2012

Kahn SR, Lim W, Dunn AS, Cushman M, Dentali F, Akl EA, Cook DJ, Balekian AA, Klein RC, Le H, Schulman S, Murad MH. American College of Chest Physicians. Prevention of VTE in nonsurgical patients: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest* 2012 Feb;**141**((2 Suppl)): 195S–226S.

Kakkos 2008

Kakkos SK, Caprini JA, Geroulakos G, Nicolaides AN, Stansby GP, Reddy DJ. Combined intermittent pneumatic leg compression and pharmacological prophylaxis for prevention of venous thromboembolism in high-risk patients. *Cochrane Database of Systematic Reviews* 2008, Issue 4. [DOI: 10.1002/14651858.CD005258.pub2]

Kelsey 2000
Kelsey LJ, Fry DM, VanderKolk WE. Thrombosis risk in the trauma patient: prevention and treatment. Hematology/ Oncology Clinics of North America April 2000; Vol. 14, issue 2:417–30.

Knudson 1994
Knudson MM, Lewis FR, Clinton A, Atkinson K, Megerman J. Prevention of venous thromboembolism in trauma patients. *Journal of Trauma-Injury Infection & Critical Care* 1994;**37**:480–7.

Knudson 1996
Knudson MM, Morabito D, Paiement GD, Shackleford S. Use of low molecular weight heparin in preventing thromboembolism in trauma patients. *Journal of Trauma-Injury Infection & Critical Care* 1996;**41**:446–59.

McMurty 1999
McMurtry AL, Owings JT, Anderson JT, Battistella FD, Gosselin R. Increased use of prophylactic vena cava filters in trauma patients failed to decrease overall incidence of pulmonary embolism. *Journal of the American College of Surgeons* 1999;**189**:314–20.

Meissner 2003
Meissner MH, Chandler WL, Elliott JS. Venous thromboembolism in trauma: a local manifestation of systemic hypercoagulability?. *Journal of Trauma-Injury Infection & Critical Care* 2003;**54**:224–31.

Nijkeuter 2004
Nijkeuter M, Huisman MV. Pentasaccharides in the prophylaxis and treatment of venous thromboembolism: a systematic review. *Current Opinion in Pulmonary Medicine* 2004;**10**(5):338–44.

O'Malley 1990
O'Malley KF, Ross SE. Pulmonary embolism in major trauma patients. *Journal of Trauma-Injury Infection & Critical Care* 1990;**30**:748–50.

RevMan 2008
The Nordic Cochrane Centre, The Cochrane Collaboration. Review Manager (RevMan). 5.0. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2008.

Rogers 1993
Rogers FB, Shackford SR, Wilson J, Ricci MA, Morris CS. Prophylactic vena cava filter insertion in severely injured trauma patients: indications and preliminary results. *Journal of Trauma-Injury Infection & Critical Care* 1993;**35**: 637–41.

Rogers 1995
Rogers FB. Venous thromboembolism in trauma patients. Surgical Clinics of North America 1995; Vol. 75:279–91.

Rogers 2002
Rogers FB, Cipolle MD, Velmahos G, Rozycki G, Luchette FA. Practice Management Guidelines for the Prevention of Venous Thromboembolism in Trauma Patients: The EAST Practice Management Guidelines Work Group. *Journal of Trauma-Injury, Infection and Critical Care* 2002;**53**(1): 142–64.

Sauaia 1995
Sauaia A, Moore FA, Moore EE, Moser KS, Brennan R, Read RA, et al.Epidemiology of trauma deaths: a reassessment. *Journal of Trauma-Injury Infection & Critical Care* 1995;**38**(2):185–93.

Sevitt 1961
Sevitt S, Gallagher N. Venous thrombosis and pulmonary embolism: a clinico-pathological study in injured and burned patients. *British Journal of Surgery* 1961;**48**:475–89.

Shackford 1988
Shackford SR, Moser KM. Deep venous thrombosis and pulmonary embolism in trauma patients. *Journal of Intensive Care Medicine* 1988;**3**:87–98.

Smith 1994
Smith RM, Airey M, Franks AJ. Death after major trauma: can we affect it? The changing cause of death in each phase after injury [abstract]. *Injury* 1994;**25**:SB23–4.

Smith 2011
Smith TO, Taylor R, Hing CB. Thromboprophylaxis following major skeletal trauma:a systematic review. *European Journal of Trauma and Emergency Surgery* 2011; **37**:479–90.

Spaniolas 2008
Spaniolas K, Velmahos GC, Wicky S, Nussbaumer K, Petrovick L, Gervasini A, et al.Is upper extremity deep venous thrombosis underdiagnosed in trauma patients?. *American Surgeon* 2008;**74**(2):124–8.

Velmahos 2000
Velmahos GC, Kern J, Chan LS, Oder D, Murray JA, Shekelle P. Prevention of venous thromboembolism after injury: an evidence-based report: Part I. Analysis of risk factors and evaluation of the role of vena caval filters. *Journal of Trauma-Injury Infection & Critical Care* 2000;**49**: 132–9.

Velmahos 2000a
Velmahos GC, Kern J, Chan LS, Oder D, Murray JA, Shekelle P. Prevention of venous thromboembolism after injury: an evidence-based report: Part II. Analysis of risk factors and evaluation of the role of vena caval filters. *Journal of Trauma-Injury Infection & Critical Care* 2000;**49**: 140–4.

WHO 2008
World Health Organization. *The global burden of disease: 2004 update*. Vol. **1**, Switzerland: WHO Library and cataloguing-data, 2008.

Wille-Jørgensen 2008
Wille-Jørgensen P, Rasmussen MS, Andersen BR, Borly L. Heparins and mechanical methods for thromboprophylaxis in colorectal surgery. *The Cochrane Library* 2008, Issue 4. [DOI: 10.1002/14651858.CD001217]

* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Anglen 1998

Methods	Randomized control trial
Participants	117 participants randomised: 49 for sequential compression device (SCD) and 68 for Plantar venous pneumatic compression (P) Gender: SCD M 38 F 30 P M 27 F 22 Mean age: SCD 38 (17-82) P 41 (18-83). Inclusion Criteria All Adult trauma with fracture of the pelvic ring, acetabulum or femur Exclusion Criteria: Inabilty of give informed consent, preexisting thrombosis, active anticoagulation,inability to use the devices Type of Injury All were blunt trauma Location of trauma: Spine: Not reported Head: Not reported Face: Not reported Chest: Not reported Abdomen: Not reported Pelvis: SCD 26 P 24 Extremity: 36 to 23 PolI-trauma (more than one): 42 to 30 Severity of trauma (ISS, RTS) not reported: Type of management (Operatory, Non operatory, both or not reported): Operatory
Interventions	thigh-calf sequential-compression device (Kendall SCD; Kendall, Mansfield, Massachusetts) PlexiPulse foot pumps (Kinetic Concepts, San Antonio, Texas)
Outcomes	Diagnostic method for DVT: Doppler ultrasonography Diagnostic method for PE: Clinically Any bleeding? No.
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	No (Medical record number).
Allocation concealment (selection bias)	High risk	No (Medical record number).
Blinding (performance bias and detection bias) All outcomes	Low risk	The scans were read by radiology in a blinded fashion.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No missing outcome data.
Selective reporting (reporting bias)	Unclear risk	Protocol not known.

Cohn 1999

Methods	Randomized control trial
Participants	66 participants randomised (32 for low dose unfractionated heparin (UH) and34 for LMWH) Gender: Not reported Mean age: 44±17 years for UH to 38±15 years for LMWH Inclusion Criteria: Any trauma patients with at least one of the following risk factors: Age > 45, expectation of > 2 days bedrest, history of DVT or PE, coma (CGS <7), spine cord injury, pelvic fracture,lower extremity fractures, and repair of mayor extremity vein, complex wound of lower extremity, femoral venous catheter Exclusion Criteria: Age < 18, sever blunt head injury, bleeding injuries no accessible to haemostatic control , active bleeding disorder, cardiovascular instability, nursing mothers, heparin, warfarin or heparinoids within 7 days of trauma, allergy of heparin, bisulphite or fish, history of protein C deficiency, history of heparin associated thrombocytopenia, malignant hypertension blood pressures over 250 systolic and 130 diastolic, liver failure with encephalopathy, renal failure or failure to obtain informed consent Type of Injury : UH Blunt: 31 Penetrating: 1 to :LMWH. Blunt 32 Penetrating:2 Location of trauma: Not reported. Severity of trauma ISS mean: UH ISS mean13+/-14 to LMWH ISS mean 10 +/- 5 Type of management (Operatory , Non operatory, both or not reported): Not reported
Interventions	UH 5000 U SC BID LMWH 30 mg SC BID
Outcomes	Diagnostic method for DVT: Doppler ultrasonography Diagnostic method for PE: Clinically, V/Q and angiograms . Any bleeding? Yes. Major Bleeding (need of transfusion, any procedure to control bleeding)
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer generated schedule.
Allocation concealment (selection bias)	Low risk	Central allocation (pharmacy-controlled randomizations).
Blinding (performance bias and detection bias) All outcomes	High risk	They don´ t say if the radiologist were blinded.
Incomplete outcome data (attrition bias) All outcomes	High risk	104 patient were randomised but at the end just 66 patient were analysed. They don´ t specify what happen with the other 42 patients
Selective reporting (reporting bias)	Unclear risk	Protocol not known.

Dennis 1993

Methods	Randomized clinical trial
Participants	395 participants randomised (281 for sequential compression device or low dose unfractionated heparin and 114 for no prophylaxis) Gender: Not reported Mean age: 28.6 years for prophylaxis to 27.4 years for no prophylaxis Inclusion Criteria: Any trauma Exclusion Criteria: Less than 18 years or ISS of 9 or below. Type of Injury (blunt , penetrated, both or not reported): Blunt: 320 Penetrating: 75. Prophylaxis: Blunt: 233 Penetrating: 48. No prophylaxis:Blunt: 87 Penetrating: 27 Location of trauma: Spine: 39 to11 Head: 74 to 18 Face: Not reported Chest: 81 to 37 Abdomen: 68 to 24 Pelvis: Not reported Extremity: 137 to 51 PolItrauma (more than one): Not reported Severity of trauma (ISS, RTS) or not reported: ISS mean: Prophylaxis: 21.1 No prophylaxis: 20.5 Type of management (Operatory , Non operatory, both or not reported): Not reported
Interventions	Prophylactic method: Full length lower extremity sequential compression device (SCD) or those who have fractures or extensive soft tissue injuries of the lower extremity and in cases where SCD were not available were given low dose of subcutaneous heparin at a dose of 5000 units BID No prophylactic method.
Outcomes	Diagnostic method for DVT: Doppler ultrasonography Diagnostic method for PE: Authopsy or Pulmonary angiography. Any bleeding ? No. Major Bleeding (need of transfusion, any procedure to control bleeding) Minor Bleeding (no need none of the above)
Notes	Less than 20% couldn't perform the duplex because of the extremity injuries. 67 where changed to prophylaxis group and analysed in the No prophylaxis group (Intervention B)

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	They were randomised, but they don´ t say how.
Allocation concealment (selection bias)	Unclear risk	They didn't describe how allocate.
Blinding (performance bias and detection bias) All outcomes	High risk	Incomplete information to establish whether the vascular technician or attending vascular surgeon were blinded37% of the 181 patients in the control group were switched from no prophylaxis to a SCD at the discretion of the attending surgeon who felt the risk of DVT and PE was too high

Dennis 1993 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	High risk	Per protocol analysis.
Selective reporting (reporting bias)	Unclear risk	All the outcomes were reported. (Protocol not known)

Elliot 1999

Methods	Randomized control trial
Participants	149 participants randomised (74 for sequential compression device (Calf thigh device) 75 for sequential compression device (Plantar venous pneumatic compression) Gender: Calf thigh device male 49 / female 25 Plantar venous pneumatic compression male 51 / female 24 Mean age: 33.9 years for Calf thigh device to 30.2 years for Plantar venous pneumatic compression Inclusion Criteria: more than 13 years old and who had recent (within 24 hours) severe head injuries (Glasgow Coma Scale score < 9) and/or major trauma and were expected to be bedridden for more than 72 hours Exclusion Criteria: Patients with external fixation devices or casts that precluded the use of calf-thigh sequential pneumatic compression devices on either or both legs, patients who were not expected to live more than 24 hours, and patients whose injuries occurred more than 24 hours before admission Type of Injury (blunt, penetrated, both or not reported): Blunt: 137 Penetrating: 12.Calf thigh device Blunt: 68 Penetrating:6. Plantar venous pneumatic compression:Blunt: 69 Penetrating: 6 Location of trauma: Spine: Not reported Head: 62 to 61 Face: 23 to 14 Chest: 39 to 44 Abdomen: 17 to 22 Pelvis: Not reported Extremity: 10 to 10 Polytrauma (more than one): Not reported Severity of trauma (ISS, RTS) or not reported: ISS mean: Calf thigh device: 31.0 Plantar venous pneumatic compression: 30.2 Type of management (Operatory, Non operatory, both or not reported): Calf thigh device Operatory 12/Non operatory 62 Plantar venous pneumatic compression Operatory 10 /Non operatory 65
Interventions	The calf-thigh sequential pneumatic compression devices consisted of four calf and two thigh plastic chambers that inflate sequentially to a pressure of 45 mm Hg. The calf chambers inflated sequentially from the ankle to the knee at 5-second intervals (as recommended by the manufacturer). The two thigh chambers then inflate sequentially in a proximal direction. All chambers remain inflated for 5 seconds, then deflate simultaneously The PlexipulseR has a single chamber that inflates for 2 seconds and cycles every 20 seconds. The chamber pressure was set to 160 mm Hg (as recommended by the manufacturer)
Outcomes	Diagnostic method for DVT: Doppler ultrasonography Diagnostic method for PE: No Any bleeding ? Yes Major Bleeding (need of transfusion, any procedure to control bleeding)

Elliot 1999 (*Continued*)

	Minor Bleeding (no need none of the above)	
Notes		

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomly assigned by computer.
Allocation concealment (selection bias)	Low risk	Individual prophylaxis assignments were written on cards and placed in sealed opaque envelopes with only the order of assignment and stratification displayed
Blinding (performance bias and detection bias) All outcomes	Low risk	They removed the calf-thigh sequential pneumatic compression devices or plantar venous intermittent pneumatic compression devices from the patient and the patient's room to maintain an assessment that was blinded to the method of venous thromboembolism prophylaxis
Incomplete outcome data (attrition bias) All outcomes	Low risk	149 patients compose the intent to treat group.
Selective reporting (reporting bias)	Unclear risk	All the outcomes were reported. (Protocol not known)

Fisher 1995

Methods	Randomized clinical Trial
Participants	304 participants randomised:145 for Pneumatico sequential leg compression devices (PSLCD) and 159 for no prophylaxis Gender: Not reported Mean age: Not reported Inclusion Criteria: Pelvic, acetabular, femoral neck, intertrochanteric or subtrochanteric fractures Exclusion Criteria: Abnormal coagulation profile, current or recent use of an antiplaquet or anticoagulant medication, malignancy, severe liver disease, skin ulceration or large open wound on lower extremity, objective evidence of DVT, severe multi-trauma in which participation of another trauma service took precedence over the study protocol Type of Injury All were blunt :PSLCD: Blunt: 145 No prophylaxis:Blunt: 154 Location of trauma: Pelvis:PSLCD 35 to No prophylaxis: 38 Extremity (hip fractures): PSLCD 110 to No prophylaxis: 121 Severity of trauma: ISS mean: Not reported Type of management : Operatory.
Interventions	PSLCD: Portable controller with a pair of thigh length sleeves. Each sleeve contains six chambers, four calf and two thigh. Sleevs were sequentially inflated to pressures of

Fisher 1995 (*Continued*)

	45 mm Hg at the ankle, 35-40 mm Hg at the calf, and 25 mm mg at the thigh.The compression cycle is 71 sec, with each compression lasting 11 sec No prophylactic method.
Outcomes	Diagnostic method for DVT: Doppler ultrasonography. Equivocal or positive tests, when indicated, were followed by venograms or autopsy Diagnostic method for PE: VQ scan, angiography or autopsy Any bleeding ? No.
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomization was by sealed enveloped and balanced in blocks of 20
Allocation concealment (selection bias)	Low risk	Sealed envelopes.
Blinding (performance bias and detection bias) All outcomes	Low risk	Diagnostic test were assessed by a blinding radiologist, vascular surgeon or nuclear medicine specialist
Incomplete outcome data (attrition bias) All outcomes	High risk	Reason for missing outcome data likely to be related to true outcome, with either imbalance in numbers or reasons for missing data across intervention groups
Selective reporting (reporting bias)	Unclear risk	All the outcomes were reported. (Protocol not known)

Fuchs 2005

Methods	Randomized clinical trial
Participants	227 participants randomised (111 Arthroflow plus unfractioned heparin and 116 for Unfractioned Heparin) Gender: Arthroflow plus unfractioned heparin M 57 F 54 Unfractioned Heparin M74 F 42 Mean age: 47.1 (19.7) years for Arthroflow plus unfractioned heparin to 71.9 (19.5) years forUnfractioned Heparin Inclusion Criteria: Above 18 and below 80 years. Bony or ligamentous trauma of spine, pelvis or extremities Exclusion Criteria: Polytrauma, decompensated coronary heart disease, advance peripheral arterial occlusion, severe liver failure, haemorraghic diathesis, stroke, pregnancy, malignant neoplasty, arthritis and arthrodesis of the lower limb, acute thrombosis or thrombophlebitis, pulmonary embolism, paraplegia, chronic muscular dystrophy, lack of compliance Type of Injury (blunt , penetrated, both or not reported): Not reported

Fuchs 2005 (*Continued*)

	Location of trauma: Spine: 40 to 30 Head: Pelvis: 27 to 20 extremities 44 to 66 Severity of trauma (ISS, RTS) or not reported: No reported Type of management (Operatory , Non operatory, both or not reported): Not reported
Interventions	Arthroflow plus UH: UH 5000 ui TID and mobilization of the extremity for 30 min TID UH 5000 ui TID
Outcomes	Diagnostic method for DVT: Doppler ultrasonography and plethysmography as screening. Confirmed diagnosis by Venography Diagnostic method for PE: Clinically Any bleeding ? Not reported.
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomly assigned by computer.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding (performance bias and detection bias) All outcomes	Low risk	Evaluated by blind radiologist.
Incomplete outcome data (attrition bias) All outcomes	High risk	Patients with trauma to the ankle had to be excluded from to the arthroflow group
Selective reporting (reporting bias)	Unclear risk	All the outcomes were reported. (Protocol not known).

Geerts 1996

Methods	Randomized clinical trial
Participants	265 participants randomised: 136 for low dose unfractionated heparin (LDUH) and 129 for LMWH Gender: LDUH male 99 / female 37 LMWH male 93 / female 36 Mean age: LDUH 37.0± 16.5 and LMWH 39.1 ± 16.8 Inclusion Criteria: Any trauma in adults. Exclusion Criteria: ISS below 9. Survival below 7 days. Hospital stay below 7 days. Intracranial bleeding by CT. Uncontrolled bleeding after 36 hours of injury. Systemic coagulopathy (PT more 3segs above control or platelets less than 50,000). Need of therapeutic anticoagulation. Contrast allergy for venography. Renal failure. Pregnant. Don´ t achieve venous access because amputation or major foot injury Type of Injury Blunt trauma

Geerts 1996 (*Continued*)

	Location of trauma: Spine: 24 to 16 Head: 6 to 7 Face: Not reported Chest:Not reported Abdomen: Not reported Pelvis: 25 to 23 Extremity: 75 to 69 Polytrauma (more than one): Not reported Severity of trauma: ISS mean: LDUH 22.7 ± 9 LMWH 23.1± 8 Type of management Operatory 119 to 107 non operatory 17 to 22
Interventions	UH 5000 ui every 12 hours (0,3 ml preloaded syringes), 36 hours after the injury and continued by 14 days. Witheld single preoperative dose and resumed dose after the surgery LMWH (Enoxaparin) 30 mg every 12 hours (0,3 ml preloaded syringes), 36 hours after the injury and continued by 14 days. Witheld single preoperative dose and resumed dose after the surgery
Outcomes	Diagnostic method for DVT:Clinical surveillance, Clinical suspect diagnosis with US-doppler and confirmation with Venography. If not (complete asymptomatic), Control Venography days 10 to 14 after injury Diagnostic method for PE: Clinical suspect with ventilation-perfusion scanning. Any doubt will be confirmed with pulmonary angiography, venous ultrasonography or contrast venography or combinations of these Any bleeding ? yes Major Bleeding (need of transfusion, any procedure to control bleeding) Minor Bleeding (no need none of the above)
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomly assigned by a computer.
Allocation concealment (selection bias)	Low risk	Blinded fashion with preloaded syringes.
Blinding (performance bias and detection bias) All outcomes	Low risk	Imaging studies and episodes of bleeding were adjudicated by a panel of experts who were unaware of the clinical data
Incomplete outcome data (attrition bias) All outcomes	Low risk	Without losses.
Selective reporting (reporting bias)	Unclear risk	Protocol not known.

Ginzburg 2003

Methods	Randomized clinical trial
Participants	442 participants randomised: 218 for LMWH and 224 for Intermitent Pneumatic Compression (IPC). Gender: 160 male for LMWH to 167 male for IPC Mean age: 42 years forLMWH to 41 years for IPC. Inclusion Criteria: Above 18 yeas old. ISS above 9. At least one leg and one arm available for the IPC. Don't need anticoagulation. Had no contraindication for LMWH Exclusion Criteria: Under 18 years. ISS under 9. Unlikely to survive or remain in hospital at least 7 days. Acute renal failure (creatinine above 3.4 mg/dL). Pregnant women. Unable to undergo bilateral duplex. Morbid obesity (>25kg/m2). Contraindication of coagulation: intracranial bleeding of uncontrolled bleeding from other sites for more than 24 hours after admission. Coaugulopathy (PT> 3s/ control or plat < 50.000) Type of Injury: Not reported. Location of trauma: Spine: 18 to 15 Head: 41 to 60 Face: 11 to 11 Chest: 80 to 92 Abdomen: 53 to 63 Pelvis: 35 to 44 Extremity: 174 to 136 PolItrauma (more than one) : Not reported Severity of trauma (ISS, RTS) or not reported: Moderately (ISS 9-19): 294.Severe (ISS >20):148 Moderate: ISS mean: LMWH: 12.4 (3.8) to IPC: 12.7 (3.9). Severe: ISS mean: LMWH: 25.3 (4.8) to IPC 25.9 (5.8). All ISS mean: ISS mean: LMWH: 16.7 (7.3) to IPC: 17. 1 (6.8) Type of management: Not reported
Interventions	LMWH (Enoxaparin): 30 mg SC BID. Begining 24h after trauma. Witheld 12h before surgery and resumed 12h after.Two doses missed IPC (Calf garment)(Huntleigh Flowtron, Manalapan, New Jersey, USA) placed both legs inflated alternately to 40 mmHg every 60 s cycle. First cycle inflated 12 s and deflated 48s. Second cycle 30 s inflated and 30 s deflated. Tolerated for up to 8 h
Outcomes	Diagnostic method for DVT: Doppler ultrasonography Diagnostic method for PE: Clinically PE or CT scan or angiography or ventilation/ perfusion scan Any bleeding ? Yes. Major Bleeding (need of transfusion, any procedure to control bleeding) Minor Bleeding (no need none of the above)
Notes	The primary endpoint, the development of significant thromboembolic complications while in hospital, served as the basis for the calculation of sample size. The protocol was designed to consider all randomised and compliant patients in the analysis. The risk of proximal DVT and pulmonary embolism in this study population was projected to be around 10 per cent in the enoxaparin group on the basis of reports from similar trials8. Enrolment of a total of 900 patients (450 in each arm) would be needed to allow the confident detection of a clinically significant 30 per cent difference in treatment efficacy between enoxaparin and IPC (power 80 per cent, one-sided significance 0·050) with an anticipated non-compliance (drop out) rate of 5 per cent. This population size was based on an expected incidence of DVT or pulmonary embolism of 20 per cent. However, at planned interim analysis (442 patients), it was realized that the incidence was only 2·0 per cent. Based on this analysis, the decision was made to cease enrolment of subjects

Ginzburg 2003 (*Continued*)

	because a tenfold increase in patient numbers would have been needed to reach significance. Because this protocol was designed to test equivalence and because LMWH has been recognized as a standard of thromboprophylaxis, use of a one-tailed test was justified

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated random.
Allocation concealment (selection bias)	Low risk	Investigators were blinded to treatment assignment before randomisation
Blinding (performance bias and detection bias) All outcomes	High risk	Single technician performed all scans. He was not blind. Also all patients were assessed daily by the investigators. Which means that investigators could see the intervention
Incomplete outcome data (attrition bias) All outcomes	High risk	Of the 442 randomised subjects 44 (15 in the IPC group and 29 in the LMWH group) were excluded from analysis because of compliance issues
Selective reporting (reporting bias)	Unclear risk	Protocol not known.

Knudson 1992

Methods	Randomized clinical trial
Participants	113 participants randomised (37 for low dose unfractionated heparin (LDUH) and 76 for Sequential pneumatic compression boots and elastic stockings (SCD and TED)) Gender: Not reported. Mean age: 37.7 ± 15.8 years for LDUH to 37.8 ± 19.4 years for SCD and TED Inclusion Criteria: Adults traumatized patients. Exclusion Criteria: Pediatric trauma patients (below 17 years), pregnant trauma patients, minor injuries, hospitalisation less than 48 hours, Type of Injury: Blunt: 91 Penetrating: 11. Location of trauma: Spine and Pelvis: 7 to 22 Head: 12 to 24 Face: Not reported Chest: 18 to 22 Abdomen: 13 to 23 Extremity: 27 to 30 PolItrauma (more than one): Not reported Severity of trauma (ISS, RTS) or not reported: ISS mean: LDUH: 15.9 ± 7.9 SCD and TED: 18.5 ± 11.8 Type of management: Not reported.
Interventions	Low Dose Unfractioned Heparin: 5000 ui SC BID. Sequential pneumatic compression boots and elastic stockings (SCD and TED)

Knudson 1992 (*Continued*)

Outcomes	Diagnostic method for DVT: Real time B mode ultrasound / 5 days for tree weeks until discharge Diagnostic method for PE: V/Q radionuclide and or pulmonary angiograms Any bleeding ? No.
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	Even and odds.
Allocation concealment (selection bias)	High risk	Alternative.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	They didn't say whether the technologist or radiologist were blinding
Incomplete outcome data (attrition bias) All outcomes	High risk	Per protocol analysis.

Knudson 1994 All groups

Methods	Randomized clinical trial
Participants	251 participants randomised in three groups: Gender: Male 200/ Female 51 Mean age: 38 years. Inclusion Criteria: Group I: Any trauma patients seriously injured. With duplex scan negative the first day before the randomising. Who could receive either of the two methods of prophylaxis Group II: Any trauma patients seriously injured. With duplex scan negative the first day before the randomising. Who could not wear bilateral devices Group III: Any trauma patients seriously injured. With duplex scan negative the first day before the randomising. Who had any contraindication to receive heparin Exclusion Criteria: Group I: Younger than 18 year old, pregnant and prisoners. Group II: Younger than 18 year old, pregnant and prisoners. Group III: Younger than 18 year old, pregnant and prisoners. Type of Injury: 140 blunt, 111 penetrating (65 stab wounds and 46 firearm) Location of trauma: Not reported. Severity of trauma: Not reported Type of management: Not reported

Knudson 1994 All groups (*Continued*)

Interventions	Group I: Low Dose Unfractioned Heparin: 5000 ui SC BID or Sequential pneumatic compression boots and elastic stockings (SCD and TED) vs Control Group II: Low Dose Unfractioned Heparin: 5000 ui SC BID vs Control Group III: Sequential pneumatic compression boots and elastic stockings (SCD and TED) vs Control
Outcomes	Diagnostic method for DVT: Dupplex. Diagnostic method for PE: V/Q and angiograms Any bleeding ? No.
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Random drawing.
Allocation concealment (selection bias)	High risk	Allocated by the possibility to wear the devices or to receive heparin
Blinding (performance bias and detection bias) All outcomes	High risk	It is not reported if the technologist or radiologist were blinded
Incomplete outcome data (attrition bias) All outcomes	High risk	145 missing patients.
Selective reporting (reporting bias)	Unclear risk	Protocol not known.

Knudson 1994 group I

Methods	
Participants	
Interventions	
Outcomes	
Notes	

Knudson 1994 group II

Methods	Randomized clinical trial
Participants	251 participants randomised in three groups: Gender: Male 200/ Female 51 Mean age: 38 years. Inclusion Criteria: Group I: Any trauma patients seriously injured. With duplex scan negative the first day before the randomising. Who could receive either of the two methods of prophylaxis Group II: Any trauma patients seriously injured. With duplex scan negative the first day before the randomising. Who could not wear bilateral devices Group III: Any trauma patients seriously injured. With duplex scan negative the first day before the randomising. Who had any contraindication to receive heparin Exclusion Criteria: Group I: Younger than 18 year old, pregnant and prisoners. Group II: Younger than 18 year old, pregnant and prisoners. Group III: Younger than 18 year old, pregnant and prisoners. Type of Injury: 140 blunt, 111 penetrating (65 stab wounds and 46 firearm) Location of trauma: Not reported. Severity of trauma: Not reported Type of management: Not reported
Interventions	Group I: Low Dose Unfractioned Heparin: 5000 u SC BID or Sequential pneumatic compression boots and elastic stockings (SCD and TED) vs Control Group II: Low Dose Unfractioned Heparin: 5000 u SC BID vs Control Group III: Sequential pneumatic compression boots and elastic stockings (SCD and TED) vs Control
Outcomes	Diagnostic method for DVT: Dupplex. Diagnostic method for PE: V/Q and angiograms Any bleeding ? No.
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Random drawing.
Allocation concealment (selection bias)	High risk	Allocated by the possibility to wear the devices or to receive heparin
Blinding (performance bias and detection bias) All outcomes	High risk	They didn´ t say weather the technologist or radiologist were blinding
Incomplete outcome data (attrition bias) All outcomes	High risk	145 missing patients.

Knudson 1994 group II (*Continued*)

Selective reporting (reporting bias)	Unclear risk	Protocol not known.

Knudson 1994 group III

Methods	Randomized clinical trial
Participants	251 participants randomised in three groups: Gender: Male 200/ Female 51 Mean age: 38 years. Inclusion Criteria: Group I: Any trauma patients seriously injured. With duplex scan negative the first day before the randomising. Who could receive either of the two methods of prophylaxis Group II: Any trauma patients seriously injured. With duplex scan negative the first day before the randomising. Who could not wear bilateral devices Group III: Any trauma patients seriously injured. With duplex scan negative the first day before the randomising. Who had any contraindication to receive heparin Exclusion Criteria: Group I: Younger than 18 year old, pregnant and prisoners. Group II: Younger than 18 year old, pregnant and prisoners. Group III: Younger than 18 year old, pregnant and prisoners. Type of Injury: 140 blunt, 111 penetrating (65 stab wounds and 46 firearm) Location of trauma: Not reported. Severity of trauma: Not reported Type of management: Not reported
Interventions	Group I: Low Dose Unfractioned Heparin: 5000 u SC BID or Sequential pneumatic compression boots and elastic stockings (SCD and TED) vs Control Group II: Low Dose Unfractioned Heparin: 5000 u SC BID vs Control Group III: Sequential pneumatic compression boots and elastic stockings (SCD and TED) vs Control
Outcomes	Diagnostic method for DVT: Dupplex. Diagnostic method for PE: V/Q and angiograms Any bleeding ? No.
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Random drawing.
Allocation concealment (selection bias)	High risk	Allocated by the possibility to wear the devices or to receive heparin

Knudson 1994 group III (*Continued*)

Blinding (performance bias and detection bias) All outcomes	High risk	They didn't say weather the technologist or radiologist were blinding
Incomplete outcome data (attrition bias) All outcomes	High risk	145 missing patients.
Selective reporting (reporting bias)	Unclear risk	Protocol not known.

Knudson 1996

Methods	Randomized clinical trial
Participants	202 participants randomised (120 for low molecular weight heparin -LMWH- and 82 for SCD or arteriovenous impulse (AVI) device) Gender: Not reported Mean age: 39 years for LMWH to 38 years for SCD and AVI. Inclusion Criteria: Injury Severity Score (ISS) of > 10 or Abbreviated Injury Scale score greater than or equal to 3 in any category; head injury with Glasgow Coma Scale score less than or equal to 8; unstable spine fracture without neurologic deficit; spine fracture with deficit; major pelvic fracture (Tile Class B or C); fracture of the lower extremity above the ankle; previous history of DVT; acute venous injury; or age >50 years Exclusion Criteria: the presence of DVT on admission, patients younger than 18 years of age, pregnant patients, prisoners, patients who could not be randomised within the first 24 hours of hospitalisation, and patients who refused consent. included discharge or transfer from the hospital before 5 days post injury, bleeding disorders possibly associated with the use of LMWH, noncompliance with the assigned prophylactic measure, or evidence of DVT on duplex examination or PE by ventilation-perfusion scan or angiography Type of Injury Blunt trauma and penetrating trauma. Location of trauma: Not reported. Severity of trauma ISS mean: LMWH 14 SCD and AVI. 16 Type of management (Operatory , Non operatory, both or not reported): Not reported
Interventions	LMWH (enoxaparin sodium, Rhone Poulenc Rorer Pharmaceuticals Inc., Collegeville, Pa) 30 mg subcutaneously every 12 hours Sequential gradient pneumatic compression (SCD) or arteriovenous impulse (AVI) device
Outcomes	Diagnostic method for DVT: venous duplex Diagnostic method for PE: Clinical observation, Arterial blood gases and oxygen saturation , three ventilation-perfusion scans and two pulmonary angiograms were performed for unexplained respiratory distress or hypoxic episodes Any bleeding ? No. Major Bleeding (need of transfusion, any procedure to control bleeding) Minor Bleeding (no need none of the above)

Knudson 1996 (*Continued*)

Notes	From 372 patients were assigned to a Heparin or a No-Heparin group, depending upon the presence of injuries that would preclude the use of heparin in the early period after injury. Just 202 patient were randomised in the heparin group to receive heparin or SCD or AVI

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated random.
Allocation concealment (selection bias)	Unclear risk	Insufficient information.
Blinding (performance bias and detection bias) All outcomes	High risk	Venous duplex examinations were performed by vascular technician with over 10 years of experience. But the article didn't say whether the vascular technician were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	The heparin group that were randomised did not have any losses
Selective reporting (reporting bias)	Unclear risk	Protocol not known.

Kurtoglu 2004

Methods	Randomized clinical trial
Participants	120 participants randomised (60 for intermittent pneumatic compressionIPC or 60 for LMWH Gender: Male 47 Female 73 Mean age: 37.1 (R 18-76) Inclusion Criteria: polytrauma with severe head/spinal injuries Exclusion Criteria: younger than 14 years old were. excluded, as were individuals with hepatic or urinary dysfunction, a spinal cord injury, a history of DVT, or a high bleeding risk (platelets < 100,000/μl or INR > 1.5) and those using anticoagulants. Patients with continuing haemorrhage on control scans within 24 hours of admission or who required craniotomy were excluded from the study Type of Injury Not reported (Blunt?). Location of trauma: Spine: 5 to 6 Head: 55 to 54 Face: Not reported Chest: Not reported Abdomen: Not reported Pelvis: Not reported Extremity: Not reported PolItrauma (more than one): Not reported Severity of trauma (ISS, RTS) or not reported: ISS mean: ISS mean Intervention A 18. 3 +/- 3.2 (4-35) Intervetion B 19.5 +/- 1.7 (4-45) Type of management (Operatory , Non operatory, both or not reported): Not reported
Interventions	IPC Intermitent pneumatic Compression the IPC patients were placed on below-knee IPC devices (Prophylactic D.V.T System, modelAC 550; Flowtron Excell, Bedfordshire, UK) or another IPC device (AV Impulse System,

Kurtoglu 2004 (*Continued*)

	Duo; Novamedix, Andover, UK) for prophylaxis LMWH group patients received enoxaparin sodium 40 mg/ day (Clexane; Aventis, Strasbourg, France
Outcomes	Diagnostic method for DVT: Venous duplex colour-flow Doppler ultrasonography of the lower extremities was obtained on admission to the ICU, each week of hospitalisation, and 1 week after discharge for all patients Diagnostic method for PE: Patients with a suspected DVT, those whose clinical status was deteriorating, and those who displayed a sudden change in blood gas levels were subjected to spiral CT scanning. Pulmonary CT examinations were undertaken with a Somatom Plus-S scanner (Siemens, Erlangen, Germany Any bleeding ? Yes Major Bleeding macroscopic hematuria without renal injury, overt bleeding, and a sudden drop in the haemoglobin level (2 g/dl) Minor Bleeding Microscopic hematuria, hematoma at the site of injection, and a drop in the haemoglobin level of less than 2 g/dl were considered minor bleeding complications
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	No (Alternate selection)
Allocation concealment (selection bias)	High risk	The patients were randomly allocated by alternate selection to either group
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Unclear (Not described)
Incomplete outcome data (attrition bias) All outcomes	Low risk	All patients randomised were analysed
Selective reporting (reporting bias)	Unclear risk	Protocol not known.

Stannard 2001

Methods	Randomized clinical trial
Participants	107 participants randomised: 54 for thigh-calf low-pressure sequential-compression device 53 for calf-foot high-pressure pulsatile-compression pump Gender: Not reported Mean age: Not reported Inclusion Criteria: blunt trauma causing a pelvic or acetabular fracture with a pattern requiring surgical fixation, an age of at

	least sixteen years, and an ability and willingness to comply with both the mechanical prophylaxis protocol and the screening studies for deep-vein thrombosis Exclusion Criteria: a history of venous thromboembolic disease, initiation of mechanical compression more than seventy-two hours following the injury, a body habitus or weight that made it difficult for the patient to fit in the magnetic resonance imaging scanner, or a stable injury that did not require surgical treatment Type of Injury: all were blunt Location of trauma: Spine: Not reported Head: Not reported Face: Not reported Chest: Not reported Abdomen: Not reported Pelvis:All were pelvis (they don´ t say how many per group Extremity: Not reported Polytrauma Not reported Severity of trauma (ISS, RTS) or not reported: ISS mean: thigh-calf low-pressure sequential-compression : 19.8 (9-59) calf-foot high-pressure pulsatile-compression pump: 16.1(9-50) Type of management Operatory
Interventions	- a thigh-calf low pressure sequential- compression device (Kendall SCD; Kendall, Mansfield, Massachusetts) - combination sequential pump that covers the calf and foot (PlexiPulse; NuTech, Kinetic Concepts, San Antonio, Texas).
Outcomes	Diagnostic method for DVT: Doppler ultrasonography and MRI venogram Diagnostic method for PE: not reported. Any bleeding ? No.
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated randomisation table.
Allocation concealment (selection bias)	Unclear risk	Not described.
Blinding (performance bias and detection bias) All outcomes	Low risk	All studies were interpreted by radiologists blinded regarding the type of prophylaxis against deep-vein thrombosis and the result of the other study
Incomplete outcome data (attrition bias) All outcomes	High risk	"Thirty-three patients who were initially enrolled in the study did not complete it. The reasons for withdrawal from the study included claustrophobia (six patients); death (six) (no patient died because of a thromboembolic event); refusal to undergo magnetic resonance venography (five); inadvertent initiation of anticoagulation by another service (five); discharge before the appropriate studies had been performed

Stannard 2001 (*Continued*)

		(three); inability of the patient to fit in the magnetic resonance scanner (two); inability of the patient to remain immobile during the magnetic resonance imaging secondary to a closed head injury (two); prior venous thromboembolic disease missed on the initial screening (two); inadvertent switching of the pump types (one); and pregnancy (one). The patients who withdrew had a total of three deep-vein thromboses, which were not included in the statistical analysis". (Stannard 2001, page 1048)
Selective reporting (reporting bias)	Unclear risk	Protocol not known.

Stannard 2006

Methods	Randomized clinical trial
Participants	200 participants randomised (Group A 97 LMWH and Group B 103 for PlexiPulse foot pump and LMWH Gender: Not reported Mean age: Group A 38.2 (19-75) Group B 41.0 (19-80) Inclusion Criteria: The inclusion criteria were blunt trauma and at least one of the following findings: an Abbreviated Injury Score of 3 or more and a long-bone fracture, multiple (two or more) long-bone fractures, or an age of more than fifty-five years and a long-bone fracture. In addition, all patients were more than eighteen years of age, had no contraindications to anticoagulation, and had been admitted to our hospital less than seventy-two hours after the time of trauma or had a negative magnetic resonance venogram prior to enrolment. Exclusion Criteria: Exclusion criteria included renal insufficiency; severe cranial or spinal cord injury; the use of anticoagulants; any contraindication to anticoagulation, including severe active bleeding; pregnancy; a history of venous thromboembolic disease; any contraindication to magnetic resonance venography; the presence of a vena cava filter; and severe ocular trauma. Cranial and ocular trauma associated with bleeding and a risk of increased intracranial or ocular pressure was considered severe and led to exclusion from the study Type of Injury Blunt trauma Location of trauma: Spine: A 2 to B 6 Head:No Face: No Chest:No Abdomen:No Pelvis: A 89 to B 85 Extremity: A 161 To B 141 PolItrauma (more than one): No Severity of trauma ISS mean:Group A 14.41 (8-57) Group B 14.43 (4-41) Type of management : Not reported
Interventions	Group A LMWH 30 mg sc BID until the discharge Group B LMWH 30 mg sc BID until the discharge and PlexiPulse foot pumps (Kinetic Concepts, San Antonio, Texas)
Outcomes	DVT Dupplex ultrasound and venous MRI before the discharge or before it was indicated MRI

Stannard 2006 (*Continued*)

Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated randomisation program.
Allocation concealment (selection bias)	Unclear risk	Not described in the full text article.
Blinding (performance bias and detection bias) All outcomes	Low risk	Two radiologists (including one of the authors , who were blinded with regard to the type of deep-vein thrombosis treatment, reviewed the coronal reformatted multiple- intensity projections and source axial images. When there was a discrepancy between the radiologists with regard to the correct interpretation, the radiologists reviewed the studies in question together and came to a consensus
Incomplete outcome data (attrition bias) All outcomes	High risk	Two hundred and twenty-four patients were enrolled, and 200 completed the entire protocol.
Selective reporting (reporting bias)	Unclear risk	Protocol not known.

Velmahos 2005

Methods	Randomized clinical trial
Participants	47 participants randomised (26 for Muscle electrostimulation (MEST) and 21 for Control) Gender: MEST: male 21/female 5 to Control: male 16/female 5 Mean age: 32 ± 15 years for MEST to 45 ± 21 years for Control Inclusion Criteria: trauma (Injury Severity Score higher than 9) and had contraindications for receiving prophylactic heparin (unfractionated or low molecular weight) were considered for inclusion in the study. Such patients were those with (a) significant head injuries, (b) operations for extensive organ injuries, (c) major retroperitoneal hematomas, (d) liver, spleen, or kidney injuries higher than Grade II, managed nonoperatively, or (e) other injuries that at the discretion of the trauma surgeon were deemed to be associated with a high likelihood for bleeding. Additional inclusion criteria were (1) anticipated survival for longer than 7 days, (2) anticipated hospital stay of longer than 7 days, and (3) randomisation within 24 hours of injury. Exclusion Criteria: a) age less than 18 years, (b) known allergy to contrast material, precluding

	the use of venography, (c) cardiac demand pacemakers or other implanted stimulators or implants containing metal parts within the area of treatment, (d) spastic paralysis, (e) local infection at the site of application, and (f) history or present evidence of venous thrombosis Type of Injury (blunt , penetrated, both or not reported): Blunt: 34 Penetrating: 13. MEST: Blunt: 18 Penetrating: 8. Control: Blunt: 16 Penetrating: 5 Location of trauma: Spine: 5 to1 Head: 7 to 1 Face: Not reported Chest: Not reported Abdomen: Not reported Pelvis: Not reported Extremity: 9 to 13 PolItrauma (more than one): Not reported Severity of trauma (ISS, RTS) or not reported: ISS mean: MEST: 20 Control: 18 Type of management (Operatory , Non operatory, both or not reported): MEST: operatory: 19 Control: operatory: 21
Interventions	Muscle electrostimulation (MEST): MEST patients received two 30-minute sessions daily, one in the morning and one in the evening, by using the Lymphavision stimulator (Bexley Trading, San Rafael, Calif). Electrodes were placed at the calves and medial thighs of both extremities. Voltage was applied gradually (0-120 V) to obtain a slight visible twitch of the muscles, usually evident by movement of the toes. Stimuli were 3 milliseconds long at a frequency of 1.75 Hz (105/minute) with inversion of polarity every 5 seconds. Daily treatments were continued for a minimum of 7 days and a maximum of 14 days. Control.
Outcomes	Diagnostic method for DVT: Venography or duplex Diagnostic method for PE: Not described Any bleeding ? None
Notes	Co-interventions:Patients of both groups were allowed to have standard prophylaxis by subcutaneous unfractionated or low-molecular-weight heparin when the contraindication for its use was no longer present (usually 3-5 days after admission) and/or by SCD if the extremities were not injured at the site of placement

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomized by a computer generated system
Allocation concealment (selection bias)	Unclear risk	Not described.

Velmahos 2005 (*Continued*)

Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not described.
Incomplete outcome data (attrition bias) All outcomes	Low risk	All randomised patients were analysed.
Selective reporting (reporting bias)	Unclear risk	Protocol not known.

Yanar 2007

Methods	Randomized clinical trial (Abstract)
Participants	120 patients three groups. They don´ t say inclusion or exclusion criteria
Interventions	Group A IPC Group B IPC +LMWH Group C LMWH
Outcomes	Diagnostic method for DVT: duplex ultrasound Diagnostic method for PE: CT Scan Any bleeding ? Not reported
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Incomplete data in the abstract.
Allocation concealment (selection bias)	Unclear risk	Incomplete data in the abstract.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Incomplete data in the abstract.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Incomplete data in the abstract.
Selective reporting (reporting bias)	Unclear risk	Protocol not known.

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Breyer 1986	Insufficient information given in the abstract to consider for inclusion
Greenfiel 1997	It is not randomised.
Haas 2003	It is an abstract and included patients with hip fractures and outpatients
Holzheimer 2004	It is a review.
Murakami 2003	DVT is not an outcome
Reilmann 1986	It is not a RCT.
Wolf 1992	It was not for trauma patients.

DATA AND ANALYSES

Comparison 1. Prophylaxis vs No prophylaxis

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Deep Venous Thrombosis (DVT)	4	997	Risk Ratio (M-H, Fixed, 95% CI)	0.52 [0.32, 0.84]
2 Pulmonary Embolism (PE)	4	997	Risk Ratio (M-H, Fixed, 95% CI)	0.65 [0.29, 1.43]
3 Mortality	4	997	Risk Ratio (M-H, Fixed, 95% CI)	0.59 [0.20, 1.70]
4 Bleeding	3	553	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Comparison 2. Mechanical prophylaxis vs No prophylaxis

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 DVT	5	907	Risk Ratio (M-H, Fixed, 95% CI)	0.55 [0.34, 0.90]
2 PE	5	907	Risk Ratio (M-H, Fixed, 95% CI)	0.77 [0.36, 1.66]
3 Mortality	5	907	Risk Ratio (M-H, Fixed, 95% CI)	0.74 [0.27, 2.04]
4 Bleeding	4	603	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Comparison 3. Pharmacological prophylaxis vs Mechanical prophylaxis

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 DVT	6	1033	Risk Ratio (M-H, Fixed, 95% CI)	0.48 [0.25, 0.95]
2 PE	6	1033	Risk Ratio (M-H, Fixed, 95% CI)	0.94 [0.36, 2.42]
3 Mortality	6	1033	Risk Ratio (M-H, Fixed, 95% CI)	1.5 [0.44, 5.16]
4 Bleeding	5	953	Risk Ratio (M-H, Fixed, 95% CI)	2.04 [1.08, 3.86]
5 Major bleeding	3	764	Risk Ratio (M-H, Fixed, 95% CI)	1.03 [0.26, 4.06]
6 Minor bleeding	3	764	Risk Ratio (M-H, Fixed, 95% CI)	2.37 [1.13, 4.98]

Comparison 4. LWMH vs UH

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 DVT	2	331	Risk Ratio (M-H, Fixed, 95% CI)	0.68 [0.50, 0.94]
2 PE	2	331	Risk Ratio (M-H, Fixed, 95% CI)	3.16 [0.13, 76.91]
3 Mortality	2	331	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Bleeding	2	331	Risk Ratio (M-H, Fixed, 95% CI)	1.63 [0.63, 4.22]
5 Major bleeding	2	331	Risk Ratio (M-H, Fixed, 95% CI)	1.46 [0.55, 3.85]
6 Minor bleeding	2	331	Risk Ratio (M-H, Fixed, 95% CI)	3.16 [0.13, 76.91]

Comparison 5. Mechanical + pharmacological prophylaxis vs Pharmacological

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 DVT	3	507	Risk Ratio (M-H, Fixed, 95% CI)	0.34 [0.19, 0.60]
2 PE	3	507	Risk Ratio (M-H, Fixed, 95% CI)	0.32 [0.05, 2.01]
3 Mortality	3	507	Risk Ratio (M-H, Fixed, 95% CI)	0.5 [0.05, 5.30]
4 Bleeding	1	200	Risk Ratio (M-H, Fixed, 95% CI)	0.99 [0.56, 1.78]

Comparison 6. Mechanical + pharmacological prophylaxis vs Mechanical prophylaxis

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 DVT	1	80	Risk Ratio (M-H, Fixed, 95% CI)	0.5 [0.10, 2.58]
2 PE	1	80	Risk Ratio (M-H, Fixed, 95% CI)	0.5 [0.05, 5.30]
3 Mortality	1	80	Risk Ratio (M-H, Fixed, 95% CI)	0.5 [0.05, 5.30]

Comparison 7. Thigh-calf vs Calf-foot

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 DVT	3	373	Risk Ratio (M-H, Fixed, 95% CI)	0.69 [0.37, 1.32]
2 PE	3	373	Risk Ratio (M-H, Fixed, 95% CI)	0.79 [0.12, 5.10]
3 Mortality	3	373	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Bleeding	3	373	Risk Ratio (M-H, Fixed, 95% CI)	3.04 [0.13, 73.44]

Comparison 8. Prophylaxis vs No prophylaxis (sensitivity analysis)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 DVT	1	304	Risk Ratio (M-H, Fixed, 95% CI)	0.37 [0.12, 1.11]
2 PE	1	304	Risk Ratio (M-H, Fixed, 95% CI)	0.73 [0.27, 2.00]

Comparison 9. Mechanical prophylaxis vs No prophylaxis (sensitivity analysis)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 DVT	1	304	Risk Ratio (M-H, Fixed, 95% CI)	0.37 [0.12, 1.11]
2 PE	1	304	Risk Ratio (M-H, Fixed, 95% CI)	0.73 [0.27, 2.00]

Comparison 10. LMWH vs UH (Sensitivity analysis)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 DVT	1	265	Risk Ratio (M-H, Fixed, 95% CI)	0.70 [0.51, 0.97]
2 PE	1	265	Risk Ratio (M-H, Fixed, 95% CI)	3.16 [0.13, 76.91]
3 Mortality	1	265	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Bleeding	1	265	Risk Ratio (M-H, Fixed, 95% CI)	5.27 [0.62, 44.51]
5 Major Bleeding	1	265	Risk Ratio (M-H, Fixed, 95% CI)	4.22 [0.48, 37.23]
6 Minor Bleeding	1	265	Risk Ratio (M-H, Fixed, 95% CI)	3.16 [0.13, 76.91]

Comparison 11. Pharmacological prophylaxis vs Mechanical prophylaxis (Sensitivity analysis)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 DVT	1	442	Risk Ratio (M-H, Fixed, 95% CI)	0.17 [0.02, 1.41]
2 PE	1	442	Risk Ratio (M-H, Fixed, 95% CI)	1.03 [0.06, 16.32]
3 Mortality	1	442	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Bleeding	1	442	Risk Ratio (M-H, Fixed, 95% CI)	1.67 [0.71, 3.95]
5 Major bleeding	1	442	Risk Ratio (M-H, Fixed, 95% CI)	1.03 [0.26, 4.06]
6 Minor bleeding	1	442	Risk Ratio (M-H, Fixed, 95% CI)	2.31 [0.72, 7.40]

Analysis 1.1. Comparison 1 Prophylaxis vs No prophylaxis, Outcome 1 Deep Venous Thrombosis (DVT).

Review: Thromboprophylaxis for trauma patients

Comparison: 1 Prophylaxis vs No prophylaxis

Outcome: 1 Deep Venous Thrombosis (DVT)

Study or subgroup	Prophylaxis n/N	No Prophylaxis n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Dennis 1993	8/281	10/114		34.7 %	0.32 [0.13, 0.80]
Fisher 1995	4/145	12/159		27.9 %	0.37 [0.12, 1.11]
Knudson 1994 All groups	6/121	9/130		21.2 %	0.72 [0.26, 1.95]
Velmahos 2005	7/26	6/21		16.2 %	0.94 [0.37, 2.38]
Total (95% CI)	**573**	**424**		**100.0 %**	**0.52 [0.32, 0.84]**

Total events: 25 (Prophylaxis), 37 (No Prophylaxis)

Heterogeneity: $Chi^2 = 3.41$, df = 3 (P = 0.33); $I^2 = 12\%$

Test for overall effect: Z = 2.67 (P = 0.0076)

Test for subgroup differences: Not applicable

Analysis 1.2. Comparison 1 Prophylaxis vs No prophylaxis, Outcome 2 Pulmonary Embolism (PE).

Review: Thromboprophylaxis for trauma patients

Comparison: 1 Prophylaxis vs No prophylaxis

Outcome: 2 Pulmonary Embolism (PE)

Study or subgroup	Prophylaxis n/N	No Prophylaxis n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Dennis 1993	2/281	2/114		19.7 %	0.41 [0.06, 2.85]
Fisher 1995	6/145	9/159		59.4 %	0.73 [0.27, 2.00]
Knudson 1994 All groups	1/121	2/130		13.3 %	0.54 [0.05, 5.85]
Velmahos 2005	1/26	1/21		7.6 %	0.81 [0.05, 12.16]
Total (95% CI)	**573**	**424**		**100.0 %**	**0.65 [0.29, 1.43]**

Total events: 10 (Prophylaxis), 14 (No Prophylaxis)

Heterogeneity: $Chi^2 = 0.33$, df = 3 (P = 0.96); $I^2 = 0.0\%$

Test for overall effect: Z = 1.07 (P = 0.28)

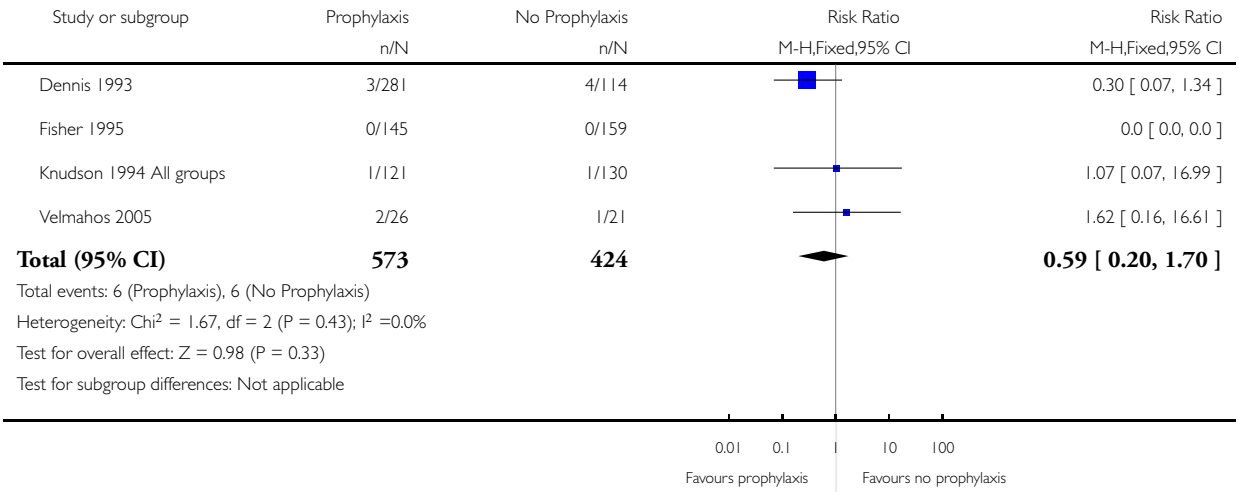
Test for subgroup differences: Not applicable

Analysis 1.3. Comparison 1 Prophylaxis vs No prophylaxis, Outcome 3 Mortality.

Review: Thromboprophylaxis for trauma patients

Comparison: 1 Prophylaxis vs No prophylaxis

Outcome: 3 Mortality



Analysis 1.4. Comparison 1 Prophylaxis vs No prophylaxis, Outcome 4 Bleeding.

Review: Thromboprophylaxis for trauma patients

Comparison: 1 Prophylaxis vs No prophylaxis

Outcome: 4 Bleeding

Study or subgroup	Prophylaxis n/N	No Prophylaxis n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Dennis 1993	0/281	0/114		0.0 [0.0, 0.0]
Knudson 1994 All groups	0/45	0/66		0.0 [0.0, 0.0]
Velmahos 2005	0/26	0/21		0.0 [0.0, 0.0]
Total (95% CI)	**352**	**201**		**0.0 [0.0, 0.0]**

Total events: 0 (Prophylaxis), 0 (No Prophylaxis)

Heterogeneity: $Chi^2 = 0.0$, df = 0 ($P<0.00001$); $I^2 = 0.0\%$

Test for overall effect: $Z = 0.0$ ($P < 0.00001$)

Test for subgroup differences: Not applicable

Analysis 2.1. Comparison 2 Mechanical prophylaxis vs No prophylaxis, Outcome 1 DVT.

Review: Thromboprophylaxis for trauma patients

Comparison: 2 Mechanical prophylaxis vs No prophylaxis

Outcome: 1 DVT

Study or subgroup	Mechanical n/N	No prophylaxis n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Knudson 1994 group I	4/32	2/64		3.5 %	4.00 [0.77, 20.69]
Knudson 1994 group III	0/26	5/39		11.6 %	0.13 [0.01, 2.34]
Velmahos 2005	7/26	6/21		17.4 %	0.94 [0.37, 2.38]
Fisher 1995	4/145	12/159		30.1 %	0.37 [0.12, 1.11]
Dennis 1993	8/281	10/114		37.4 %	0.32 [0.13, 0.80]
Total (95% CI)	**510**	**397**		**100.0 %**	**0.55 [0.34, 0.90]**

Total events: 23 (Mechanical), 35 (No prophylaxis)

Heterogeneity: $Chi^2 = 9.66$, df = 4 (P = 0.05); $I^2 = 59\%$

Test for overall effect: Z = 2.40 (P = 0.016)

Test for subgroup differences: Not applicable

Analysis 2.2. Comparison 2 Mechanical prophylaxis vs No prophylaxis, Outcome 2 PE.

Review: Thromboprophylaxis for trauma patients

Comparison: 2 Mechanical prophylaxis vs No prophylaxis

Outcome: 2 PE

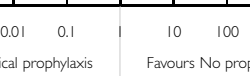
Study or subgroup	Mechanical n/N	No prophylaxis n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Dennis 1993	2/281	2/114		20.4 %	0.41 [0.06, 2.85]
Fisher 1995	6/145	9/159		61.5 %	0.73 [0.27, 2.00]
Knudson 1994 group I	0/32	1/64		7.2 %	0.66 [0.03, 15.68]
Knudson 1994 group III	1/26	0/39		2.9 %	4.44 [0.19, 105.09]
Velmahos 2005	1/26	1/21		7.9 %	0.81 [0.05, 12.16]
Total (95% CI)	**510**	**397**		**100.0 %**	**0.77 [0.36, 1.66]**

Total events: 10 (Mechanical), 13 (No prophylaxis)

Heterogeneity: Chi^2 = 1.62, df = 4 (P = 0.81); I^2 =0.0%

Test for overall effect: Z = 0.66 (P = 0.51)

Test for subgroup differences: Not applicable

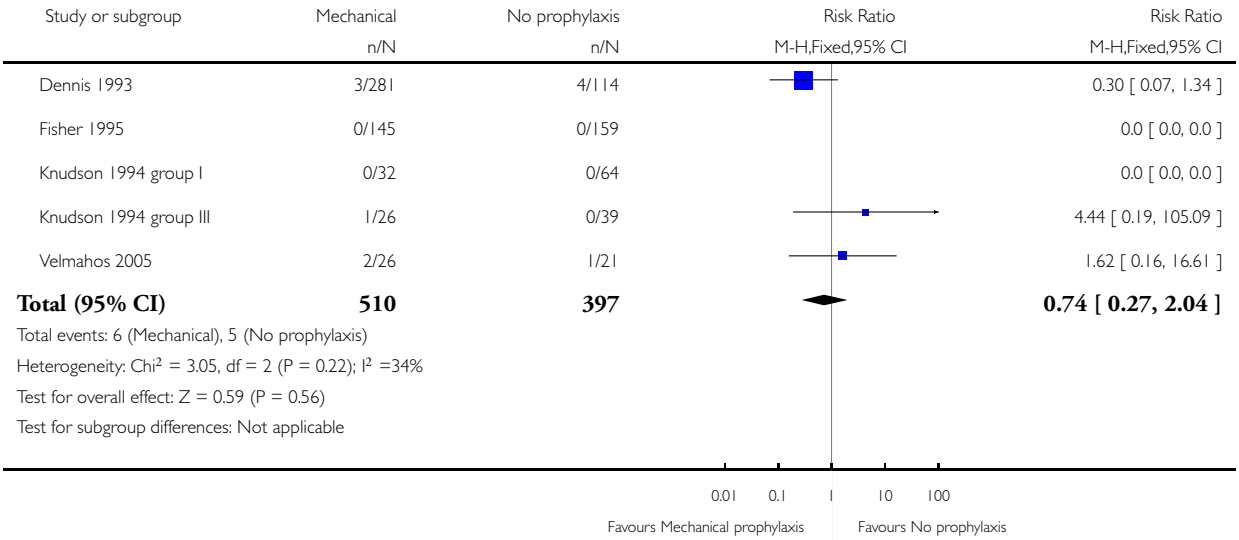


Analysis 2.3. Comparison 2 Mechanical prophylaxis vs No prophylaxis, Outcome 3 Mortality.

Review: Thromboprophylaxis for trauma patients

Comparison: 2 Mechanical prophylaxis vs No prophylaxis

Outcome: 3 Mortality



Analysis 2.4. Comparison 2 Mechanical prophylaxis vs No prophylaxis, Outcome 4 Bleeding.

Review: Thromboprophylaxis for trauma patients

Comparison: 2 Mechanical prophylaxis vs No prophylaxis

Outcome: 4 Bleeding

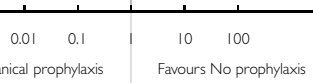
Study or subgroup	Mechanical n/N	No prophylaxis n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Velmahos 2005	0/26	0/21		0.0 [0.0, 0.0]
Knudson 1994 group I	0/32	0/64		0.0 [0.0, 0.0]
Dennis 1993	0/281	0/114		0.0 [0.0, 0.0]
Knudson 1994 group III	0/26	0/39		0.0 [0.0, 0.0]
Total (95% CI)	**365**	**238**		**0.0 [0.0, 0.0]**

Total events: 0 (Mechanical), 0 (No prophylaxis)

Heterogeneity: $Chi^2 = 0.0$, $df = 0$ ($P<0.00001$); $I^2 = 0.0\%$

Test for overall effect: $Z = 0.0$ ($P < 0.00001$)

Test for subgroup differences: Not applicable



Analysis 3.1. Comparison 3 Pharmacological prophylaxis vs Mechanical prophylaxis, Outcome 1 DVT.

Review: Thromboprophylaxis for trauma patients

Comparison: 3 Pharmacological prophylaxis vs Mechanical prophylaxis

Outcome: 1 DVT

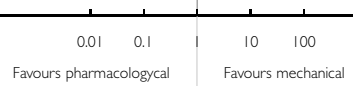
Study or subgroup	Pharmacologycal n/N	Mechanical n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Ginzburg 2003	1/218	6/224		24.5 %	0.17 [0.02, 1.41]
Knudson 1992	3/37	5/76		13.5 %	1.23 [0.31, 4.88]
Knudson 1994 group 1	1/44	4/32		19.1 %	0.18 [0.02, 1.55]
Knudson 1996	1/120	2/82		9.8 %	0.34 [0.03, 3.71]
Kurtoglu 2004	3/60	4/60		16.5 %	0.75 [0.18, 3.21]
Yanar 2007	2/40	4/40		16.5 %	0.50 [0.10, 2.58]
Total (95% CI)	**519**	**514**		**100.0 %**	**0.48 [0.25, 0.95]**

Total events: 11 (Pharmacologycal), 25 (Mechanical)

Heterogeneity: $Chi^2 = 3.94$, df = 5 (P = 0.56); $I^2 = 0.0\%$

Test for overall effect: Z = 2.12 (P = 0.034)

Test for subgroup differences: Not applicable

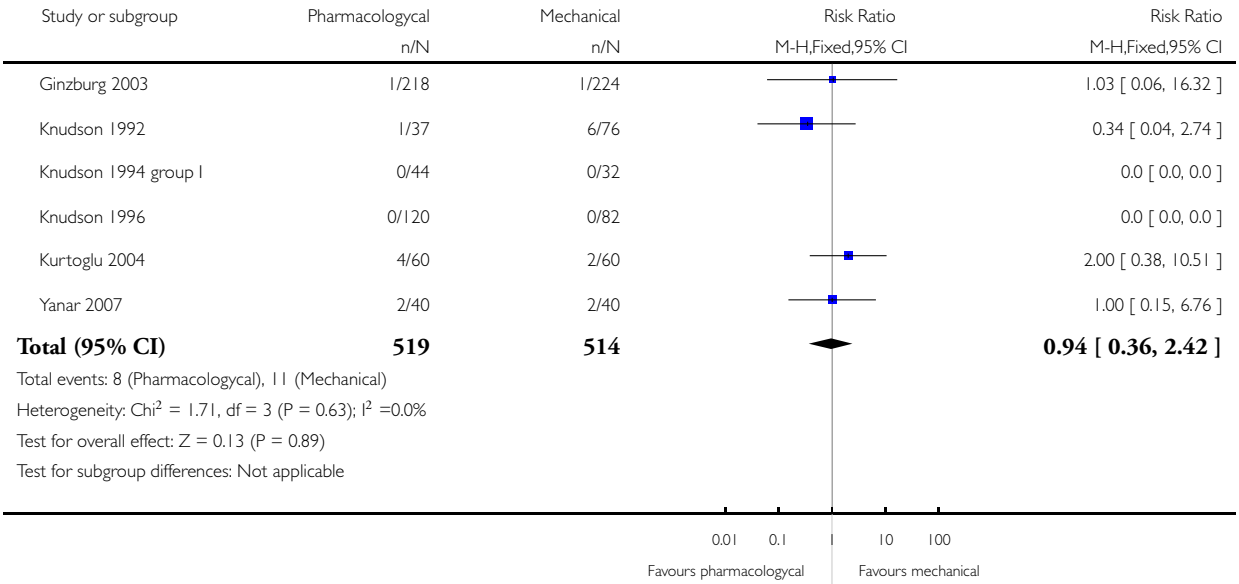


Analysis 3.2. Comparison 3 Pharmacological prophylaxis vs Mechanical prophylaxis, Outcome 2 PE.

Review: Thromboprophylaxis for trauma patients

Comparison: 3 Pharmacological prophylaxis vs Mechanical prophylaxis

Outcome: 2 PE



Analysis 3.3. Comparison 3 Pharmacological prophylaxis vs Mechanical prophylaxis, Outcome 3 Mortality.

Review: Thromboprophylaxis for trauma patients

Comparison: 3 Pharmacological prophylaxis vs Mechanical prophylaxis

Outcome: 3 Mortality

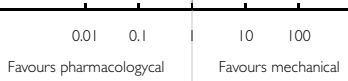
Study or subgroup	Pharmacologycal n/N	Mechanical n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Ginzburg 2003	0/218	0/224		0.0 [0.0, 0.0]
Knudson 1992	0/37	0/76		0.0 [0.0, 0.0]
Knudson 1994 group I	0/44	0/32		0.0 [0.0, 0.0]
Knudson 1996	0/120	0/82		0.0 [0.0, 0.0]
Kurtoglu 2004	4/60	2/60		2.00 [0.38, 10.51]
Yanar 2007	2/40	2/40		1.00 [0.15, 6.76]
Total (95% CI)	**519**	**514**		**1.50 [0.44, 5.16]**

Total events: 6 (Pharmacologycal), 4 (Mechanical)

Heterogeneity: $Chi^2 = 0.29$, df = 1 (P = 0.59); $I^2 = 0.0\%$

Test for overall effect: Z = 0.64 (P = 0.52)

Test for subgroup differences: Not applicable



Analysis 3.4. Comparison 3 Pharmacological prophylaxis vs Mechanical prophylaxis, Outcome 4 Bleeding.

Review: Thromboprophylaxis for trauma patients

Comparison: 3 Pharmacological prophylaxis vs Mechanical prophylaxis

Outcome: 4 Bleeding

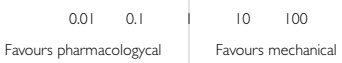
Study or subgroup	Pharmacologycal n/N	Mechanical n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Ginzburg 2003	13/218	8/224		1.67 [0.71, 3.95]
Knudson 1992	0/37	0/76		0.0 [0.0, 0.0]
Knudson 1994 group I	0/44	0/32		0.0 [0.0, 0.0]
Knudson 1996	6/120	0/82		8.92 [0.51, 156.15]
Kurtoglu 2004	9/60	5/60		1.80 [0.64, 5.06]
Total (95% CI)	**479**	**474**		**2.04 [1.08, 3.86]**

Total events: 28 (Pharmacologycal), 13 (Mechanical)

Heterogeneity: $Chi^2 = 1.28$, df = 2 (P = 0.53); $I^2 = 0.0\%$

Test for overall effect: Z = 2.19 (P = 0.029)

Test for subgroup differences: Not applicable



Analysis 3.5. Comparison 3 Pharmacological prophylaxis vs Mechanical prophylaxis, Outcome 5 Major bleeding.

Review: Thromboprophylaxis for trauma patients

Comparison: 3 Pharmacological prophylaxis vs Mechanical prophylaxis

Outcome: 5 Major bleeding

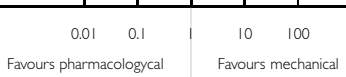
Study or subgroup	Pharmacologycal n/N	Mechanical n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Ginzburg 2003	4/218	4/224		1.03 [0.26, 4.06]
Knudson 1996	0/120	0/82		0.0 [0.0, 0.0]
Kurtoglu 2004	0/60	0/60		0.0 [0.0, 0.0]
Total (95% CI)	**398**	**366**		**1.03 [0.26, 4.06]**

Total events: 4 (Pharmacologycal), 4 (Mechanical)

Heterogeneity: $Chi^2 = 0.0$, df = 0 (P = 1.00); $I^2 = 0.0\%$

Test for overall effect: Z = 0.04 (P = 0.97)

Test for subgroup differences: Not applicable



Analysis 3.6. Comparison 3 Pharmacological prophylaxis vs Mechanical prophylaxis, Outcome 6 Minor bleeding.

Review: Thromboprophylaxis for trauma patients

Comparison: 3 Pharmacological prophylaxis vs Mechanical prophylaxis

Outcome: 6 Minor bleeding

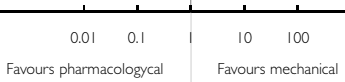
Study or subgroup	Pharmacologycal n/N	Mechanical n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Ginzburg 2003	9/218	4/224		41.4 %	2.31 [0.72, 7.40]
Knudson 1996	5/120	0/82		6.2 %	7.55 [0.42, 134.63]
Kurtoglu 2004	9/60	5/60		52.4 %	1.80 [0.64, 5.06]
Total (95% CI)	**398**	**366**		**100.0 %**	**2.37 [1.13, 4.98]**

Total events: 23 (Pharmacologycal), 9 (Mechanical)

Heterogeneity: $Chi^2 = 0.89$, df = 2 (P = 0.64); $I^2 = 0.0\%$

Test for overall effect: Z = 2.28 (P = 0.023)

Test for subgroup differences: Not applicable



Analysis 4.1. Comparison 4 LWMH vs UH, Outcome 1 DVT.

Review: Thromboprophylaxis for trauma patients

Comparison: 4 LWMH vs UH

Outcome: 1 DVT

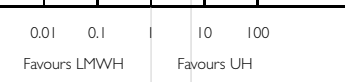
Study or subgroup	LMWH n/N	UH n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Cohn 1999	0/34	2/32		4.2 %	0.19 [0.01, 3.78]
Geerts 1996	40/129	60/136		95.8 %	0.70 [0.51, 0.97]
Total (95% CI)	**163**	**168**		**100.0 %**	**0.68 [0.50, 0.94]**

Total events: 40 (LMWH), 62 (UH)

Heterogeneity: $Chi^2 = 0.74$, df = 1 (P = 0.39); $I^2 = 0.0\%$

Test for overall effect: Z = 2.37 (P = 0.018)

Test for subgroup differences: Not applicable



Analysis 4.2. Comparison 4 LWMH vs UH, Outcome 2 PE.

Review: Thromboprophylaxis for trauma patients

Comparison: 4 LWMH vs UH

Outcome: 2 PE

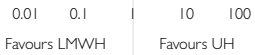
Study or subgroup	LMWH n/N	UH n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Cohn 1999	0/34	0/32		0.0 [0.0, 0.0]
Geerts 1996	1/129	0/136		3.16 [0.13, 76.91]
Total (95% CI)	**163**	**168**		**3.16 [0.13, 76.91]**

Total events: 1 (LMWH), 0 (UH)

Heterogeneity: Chi^2 = 0.0, df = 0 (P = 1.00); I^2 =0.0%

Test for overall effect: Z = 0.71 (P = 0.48)

Test for subgroup differences: Not applicable



Analysis 4.3. Comparison 4 LWMH vs UH, Outcome 3 Mortality.

Review: Thromboprophylaxis for trauma patients

Comparison: 4 LWMH vs UH

Outcome: 3 Mortality

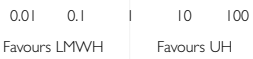
Study or subgroup	LMWH n/N	UH n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Cohn 1999	0/34	0/32		0.0 [0.0, 0.0]
Geerts 1996	0/129	0/136		0.0 [0.0, 0.0]
Total (95% CI)	**163**	**168**		**0.0 [0.0, 0.0]**

Total events: 0 (LMWH), 0 (UH)

Heterogeneity: Chi² = 0.0, df = 0 (P<0.00001); I² =0.0%

Test for overall effect: Z = 0.0 (P < 0.00001)

Test for subgroup differences: Not applicable



Analysis 4.4. Comparison 4 LWMH vs UH, Outcome 4 Bleeding.

Review: Thromboprophylaxis for trauma patients

Comparison: 4 LWMH vs UH

Outcome: 4 Bleeding

Study or subgroup	LMWH n/N	UH n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Cohn 1999	5/34	5/32		84.1 %	0.94 [0.30, 2.95]
Geerts 1996	5/129	1/136		15.9 %	5.27 [0.62, 44.51]
Total (95% CI)	**163**	**168**		**100.0 %**	**1.63 [0.63, 4.22]**

Total events: 10 (LMWH), 6 (UH)

Heterogeneity: Chi² = 2.05, df = 1 (P = 0.15); I² =51%

Test for overall effect: Z = 1.01 (P = 0.31)

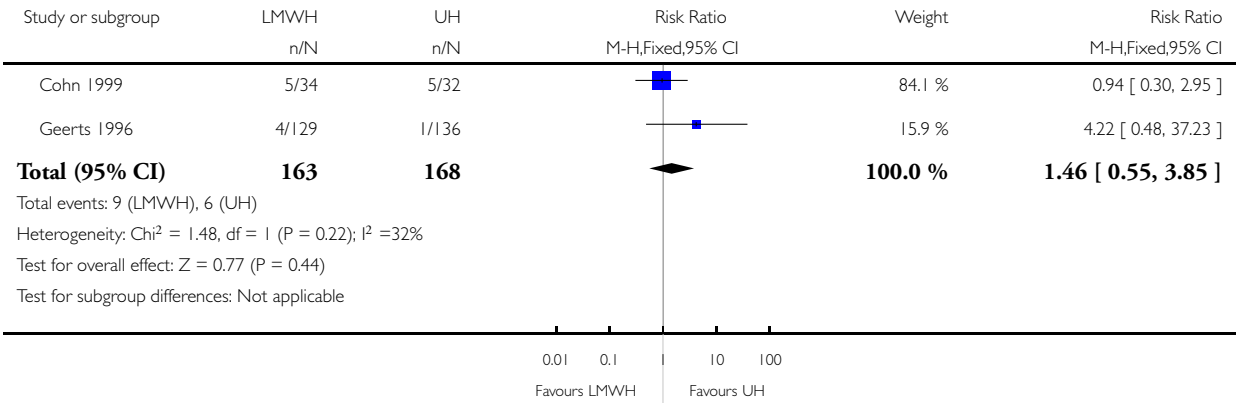
Test for subgroup differences: Not applicable

Analysis 4.5. Comparison 4 LWMH vs UH, Outcome 5 Major bleeding.

Review: Thromboprophylaxis for trauma patients

Comparison: 4 LWMH vs UH

Outcome: 5 Major bleeding

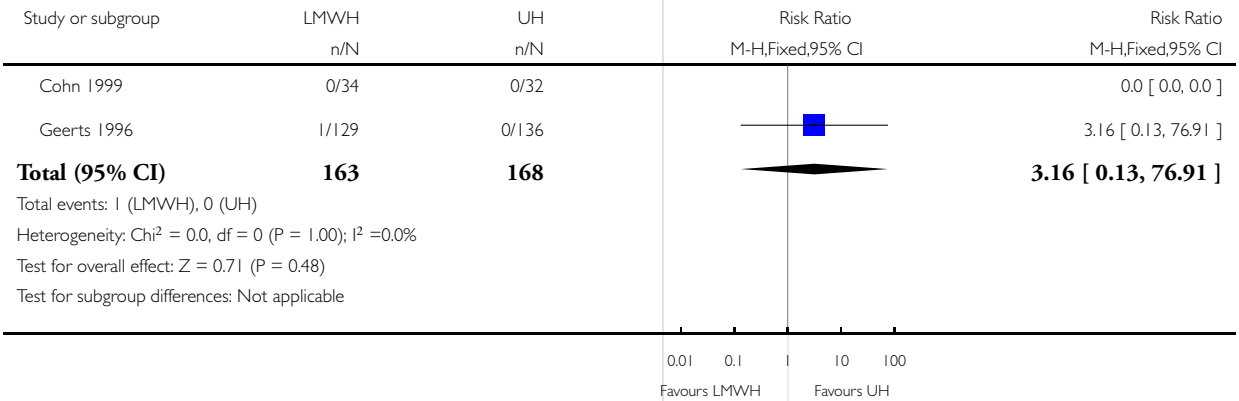


Analysis 4.6. Comparison 4 LWMH vs UH, Outcome 6 Minor bleeding.

Review: Thromboprophylaxis for trauma patients

Comparison: 4 LWMH vs UH

Outcome: 6 Minor bleeding



Analysis 5.1. Comparison 5 Mechanical + pharmacological prophylaxis vs Pharmacological, Outcome 1 DVT.

Review: Thromboprophylaxis for trauma patients

Comparison: 5 Mechanical + pharmacological prophylaxis vs Pharmacological

Outcome: 1 DVT

Study or subgroup	Mechanical plus pharmacologycal prophylaxis n/N	Pharmacologycal n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Fuchs 2005	4/111	29/116		64.8 %	0.14 [0.05, 0.40]
Stannard 2006	9/103	13/97		30.6 %	0.65 [0.29, 1.46]
Yanar 2007	2/40	2/40		4.6 %	1.00 [0.15, 6.76]
Total (95% CI)	**254**	**253**		**100.0 %**	**0.34 [0.19, 0.60]**

Total events: 15 (Mechanical plus pharmacologycal prophylaxis), 44 (Pharmacologycal)

Heterogeneity: $Chi^2 = 6.52$, df = 2 (P = 0.04); $I^2 = 69\%$

Test for overall effect: Z = 3.74 (P = 0.00019)

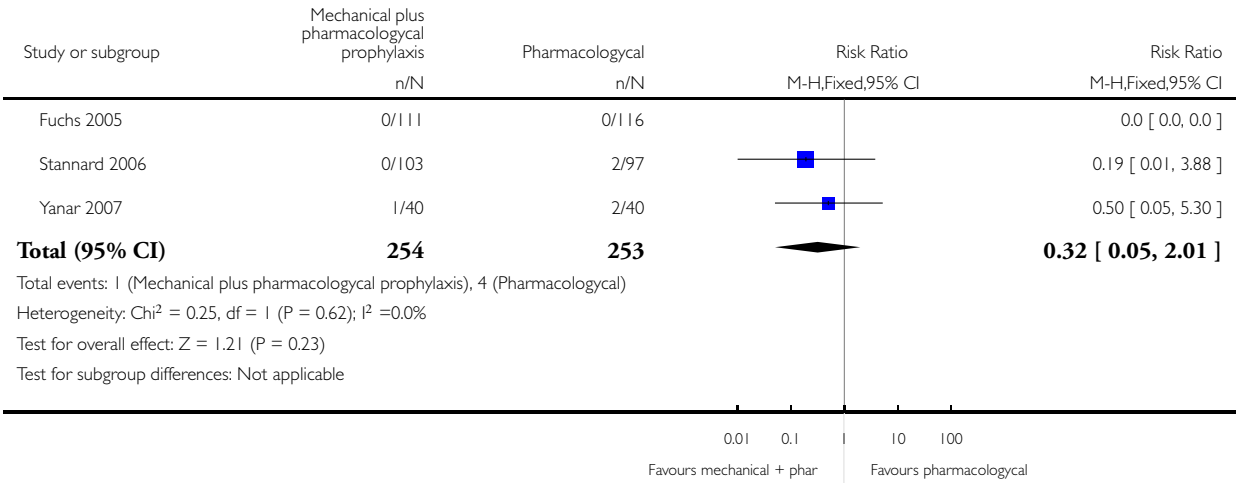
Test for subgroup differences: Not applicable

Analysis 5.2. Comparison 5 Mechanical + pharmacological prophylaxis vs Pharmacological, Outcome 2 PE.

Review: Thromboprophylaxis for trauma patients

Comparison: 5 Mechanical + pharmacological prophylaxis vs Pharmacological

Outcome: 2 PE



Analysis 5.3. Comparison 5 Mechanical + pharmacological prophylaxis vs Pharmacological, Outcome 3 Mortality.

Review: Thromboprophylaxis for trauma patients

Comparison: 5 Mechanical + pharmacological prophylaxis vs Pharmacological

Outcome: 3 Mortality

Study or subgroup	Mechanical plus pharmacologycal prophylaxis n/N	Pharmacologycal n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Fuchs 2005	0/111	0/116		0.0 [0.0, 0.0]
Stannard 2006	0/103	0/97		0.0 [0.0, 0.0]
Yanar 2007	1/40	2/40		0.50 [0.05, 5.30]
Total (95% CI)	**254**	**253**		**0.50 [0.05, 5.30]**

Total events: 1 (Mechanical plus pharmacologycal prophylaxis), 2 (Pharmacologycal)

Heterogeneity: $Chi^2 = 0.0$, df = 0 (P = 1.00); $I^2 = 0.0\%$

Test for overall effect: Z = 0.58 (P = 0.56)

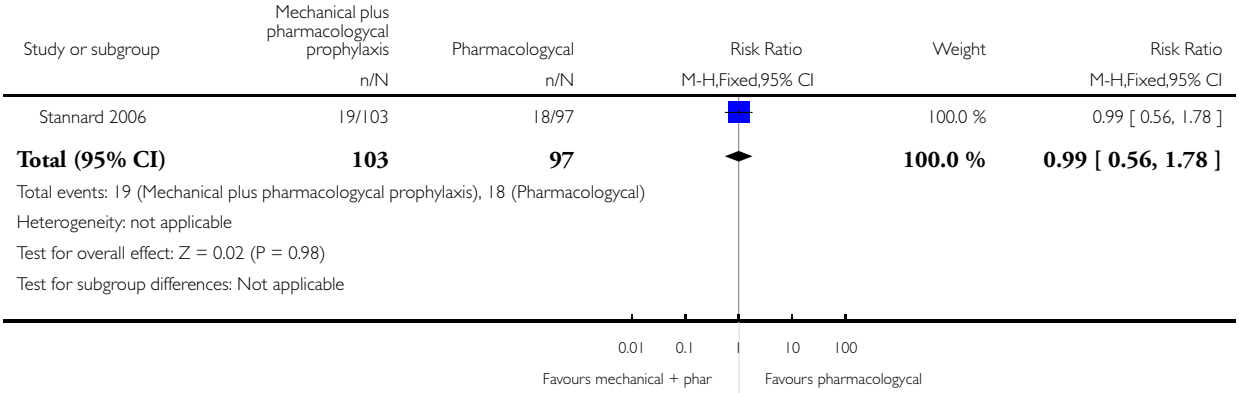
Test for subgroup differences: Not applicable

Analysis 5.4. Comparison 5 Mechanical + pharmacological prophylaxis vs Pharmacological, Outcome 4 Bleeding.

Review: Thromboprophylaxis for trauma patients

Comparison: 5 Mechanical + pharmacological prophylaxis vs Pharmacological

Outcome: 4 Bleeding

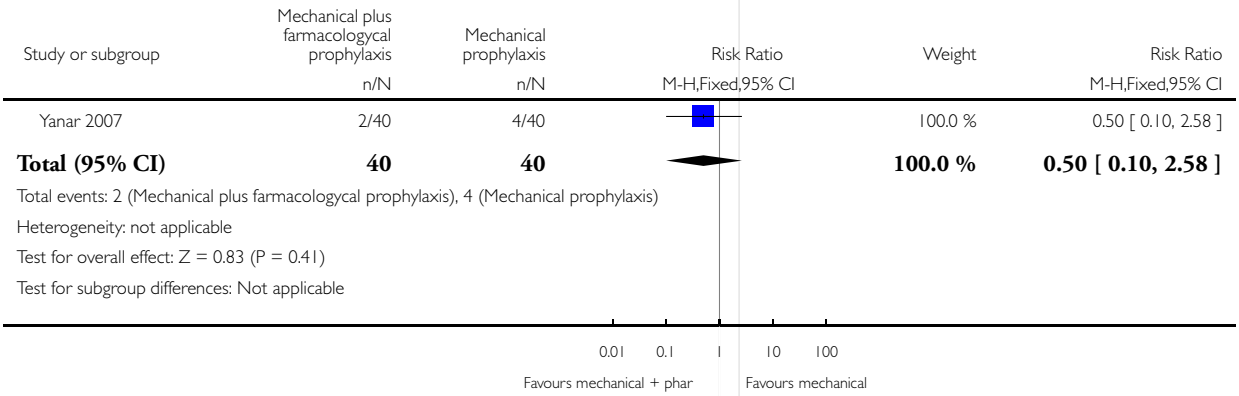


Analysis 6.1. Comparison 6 Mechanical + pharmacological prophylaxis vs Mechanical prophylaxis, Outcome 1 DVT.

Review: Thromboprophylaxis for trauma patients

Comparison: 6 Mechanical + pharmacological prophylaxis vs Mechanical prophylaxis

Outcome: 1 DVT

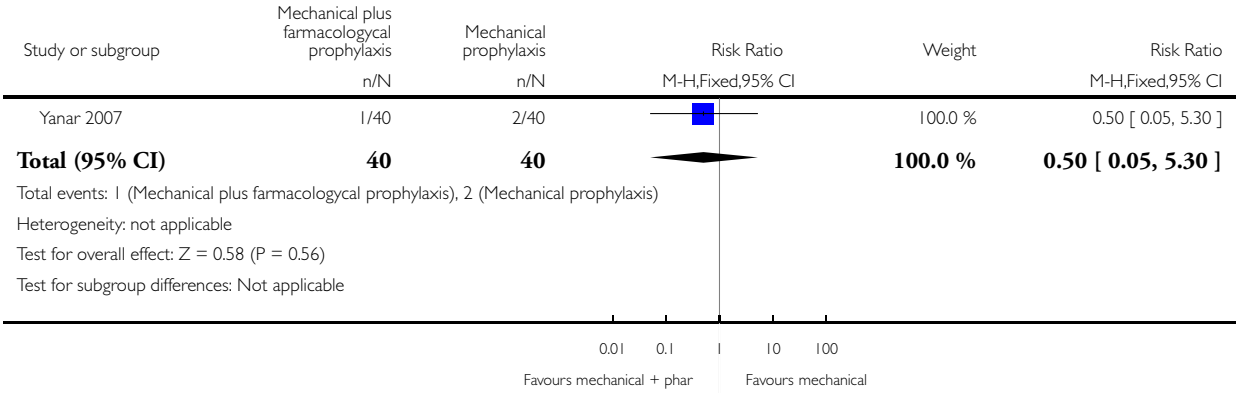


Analysis 6.2. Comparison 6 Mechanical + pharmacological prophylaxis vs Mechanical prophylaxis, Outcome 2 PE.

Review: Thromboprophylaxis for trauma patients

Comparison: 6 Mechanical + pharmacological prophylaxis vs Mechanical prophylaxis

Outcome: 2 PE

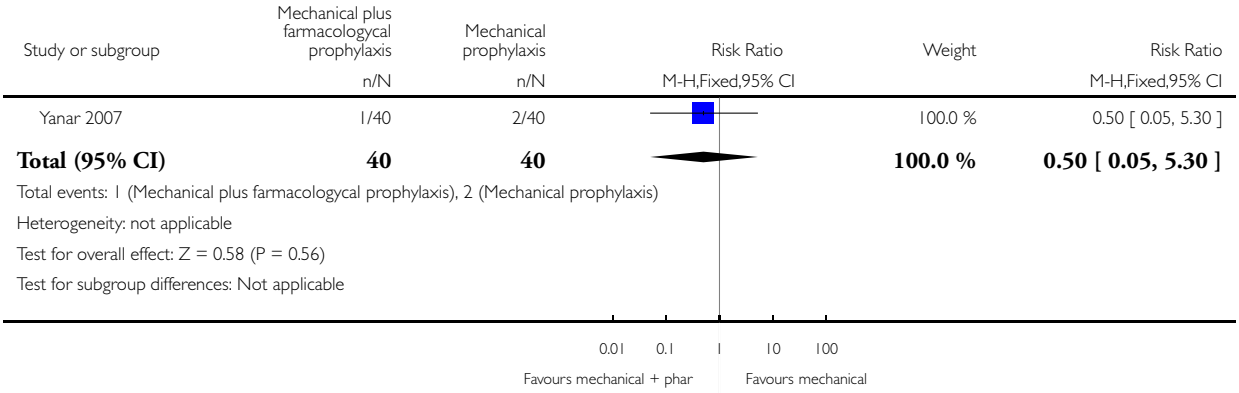


Analysis 6.3. Comparison 6 Mechanical + pharmacological prophylaxis vs Mechanical prophylaxis, Outcome 3 Mortality.

Review: Thromboprophylaxis for trauma patients

Comparison: 6 Mechanical + pharmacological prophylaxis vs Mechanical prophylaxis

Outcome: 3 Mortality

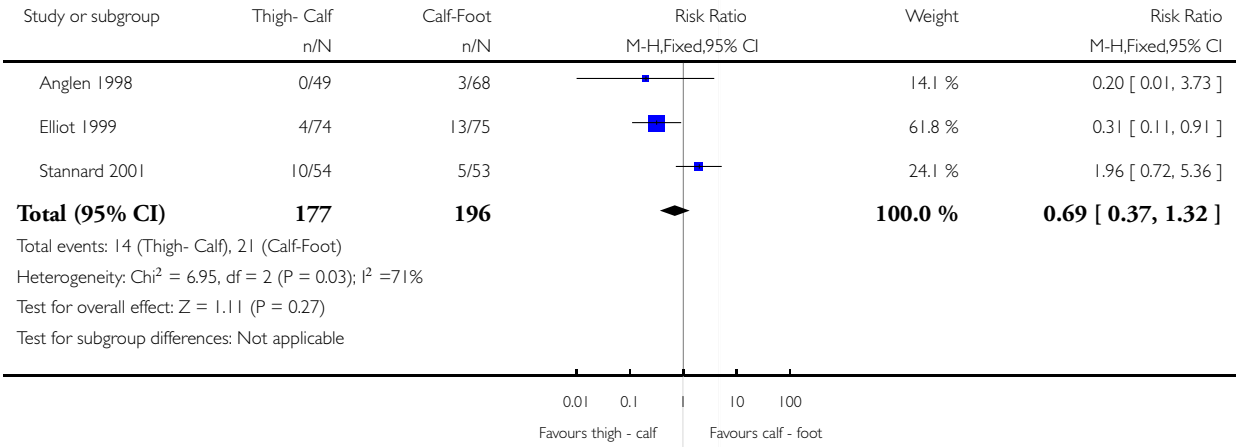


Analysis 7.1. Comparison 7 Thigh-calf vs Calf-foot, Outcome 1 DVT.

Review: Thromboprophylaxis for trauma patients

Comparison: 7 Thigh-calf vs Calf-foot

Outcome: 1 DVT



Analysis 7.2. Comparison 7 Thigh-calf vs Calf-foot, Outcome 2 PE.

Review: Thromboprophylaxis for trauma patients

Comparison: 7 Thigh-calf vs Calf-foot

Outcome: 2 PE

Study or subgroup	Thigh- Calf n/N	Calf-Foot n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Anglen 1998	0/49	2/68		0.28 [0.01, 5.62]
Elliot 1999	0/74	0/75		0.0 [0.0, 0.0]
Stannard 2001	1/54	0/53		2.95 [0.12, 70.72]
Total (95% CI)	**177**	**196**		**0.79 [0.12, 5.10]**

Total events: 1 (Thigh- Calf), 2 (Calf-Foot)

Heterogeneity: Chi^2 = 1.13, df = 1 (P = 0.29); I^2 =11%

Test for overall effect: Z = 0.24 (P = 0.81)

Test for subgroup differences: Not applicable

Analysis 7.3. Comparison 7 Thigh-calf vs Calf-foot, Outcome 3 Mortality.

Review: Thromboprophylaxis for trauma patients

Comparison: 7 Thigh-calf vs Calf-foot

Outcome: 3 Mortality

Study or subgroup	Thigh- Calf n/N	Calf-Foot n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Anglen 1998	0/49	0/68		0.0 [0.0, 0.0]
Elliot 1999	0/74	0/75		0.0 [0.0, 0.0]
Stannard 2001	0/54	0/53		0.0 [0.0, 0.0]
Total (95% CI)	**177**	**196**		**0.0 [0.0, 0.0]**

Total events: 0 (Thigh- Calf), 0 (Calf-Foot)

Heterogeneity: Chi^2 = 0.0, df = 0 (P<0.00001); I^2 =0.0%

Test for overall effect: Z = 0.0 (P < 0.00001)

Test for subgroup differences: Not applicable

Analysis 7.4. Comparison 7 Thigh-calf vs Calf-foot, Outcome 4 Bleeding.

Review: Thromboprophylaxis for trauma patients

Comparison: 7 Thigh-calf vs Calf-foot

Outcome: 4 Bleeding

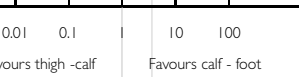
Study or subgroup	Thigh- Calf n/N	Calf-Foot n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Anglen 1998	0/49	0/68		0.0 [0.0, 0.0]
Elliot 1999	1/74	0/75		3.04 [0.13, 73.44]
Stannard 2001	0/54	0/53		0.0 [0.0, 0.0]
Total (95% CI)	**177**	**196**		**3.04 [0.13, 73.44]**

Total events: 1 (Thigh- Calf), 0 (Calf-Foot)

Heterogeneity: Chi^2 = 0.0, df = 0 (P = 1.00); I^2 =0.0%

Test for overall effect: Z = 0.68 (P = 0.49)

Test for subgroup differences: Not applicable



Analysis 8.1. Comparison 8 Prophylaxis vs No prophylaxis (sensitivity analysis), Outcome 1 DVT.

Review: Thromboprophylaxis for trauma patients

Comparison: 8 Prophylaxis vs No prophylaxis (sensitivity analysis)

Outcome: 1 DVT

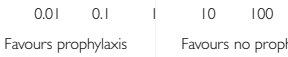
Study or subgroup	Prophylaxis n/N	No prophylaxis n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Fisher 1995	4/145	12/159		100.0 %	0.37 [0.12, 1.11]
Total (95% CI)	**145**	**159**		**100.0 %**	**0.37 [0.12, 1.11]**

Total events: 4 (Prophylaxis), 12 (No prophylaxis)

Heterogeneity: not applicable

Test for overall effect: Z = 1.78 (P = 0.075)

Test for subgroup differences: Not applicable



Analysis 8.2. Comparison 8 Prophylaxis vs No prophylaxis (sensitivity analysis), Outcome 2 PE.

Review: Thromboprophylaxis for trauma patients

Comparison: 8 Prophylaxis vs No prophylaxis (sensitivity analysis)

Outcome: 2 PE

Study or subgroup	Prophylaxis n/N	No prophylaxis n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Fisher 1995	6/145	9/159		100.0 %	0.73 [0.27, 2.00]
Total (95% CI)	**145**	**159**		**100.0 %**	**0.73 [0.27, 2.00]**

Total events: 6 (Prophylaxis), 9 (No prophylaxis)
Heterogeneity: not applicable
Test for overall effect: Z = 0.61 (P = 0.54)
Test for subgroup differences: Not applicable

Analysis 9.1. Comparison 9 Mechanical prophylaxis vs No prophylaxis (sensitivity analysis), Outcome 1 DVT.

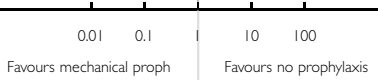
Review: Thromboprophylaxis for trauma patients

Comparison: 9 Mechanical prophylaxis vs No prophylaxis (sensitivity analysis)

Outcome: 1 DVT

Study or subgroup	Mechanical n/N	No prophylaxis n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Fisher 1995	4/145	12/159		100.0 %	0.37 [0.12, 1.11]
Total (95% CI)	**145**	**159**		**100.0 %**	**0.37 [0.12, 1.11]**

Total events: 4 (Mechanical), 12 (No prophylaxis)
Heterogeneity: not applicable
Test for overall effect: Z = 1.78 (P = 0.075)
Test for subgroup differences: Not applicable



Analysis 9.2. Comparison 9 Mechanical prophylaxis vs No prophylaxis (sensitivity analysis), Outcome 2 PE.

Review: Thromboprophylaxis for trauma patients

Comparison: 9 Mechanical prophylaxis vs No prophylaxis (sensitivity analysis)

Outcome: 2 PE

Study or subgroup	Mechanical n/N	No prophylaxis n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Fisher 1995	6/145	9/159		100.0 %	0.73 [0.27, 2.00]
Total (95% CI)	**145**	**159**		**100.0 %**	**0.73 [0.27, 2.00]**

Total events: 6 (Mechanical), 9 (No prophylaxis)
Heterogeneity: not applicable
Test for overall effect: Z = 0.61 (P = 0.54)
Test for subgroup differences: Not applicable

Analysis 10.1. Comparison 10 LMWH vs UH (Sensitivity analysis), Outcome 1 DVT.

Review: Thromboprophylaxis for trauma patients

Comparison: 10 LMWH vs UH (Sensitivity analysis)

Outcome: 1 DVT

Study or subgroup	LMWH n/N	UH n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Geerts 1996	40/129	60/136		100.0 %	0.70 [0.51, 0.97]
Total (95% CI)	**129**	**136**		**100.0 %**	**0.70 [0.51, 0.97]**

Total events: 40 (LMWH), 60 (UH)
Heterogeneity: not applicable
Test for overall effect: Z = 2.16 (P = 0.030)
Test for subgroup differences: Not applicable

Analysis 10.2. Comparison 10 LMWH vs UH (Sensitivity analysis), Outcome 2 PE.

Review: Thromboprophylaxis for trauma patients

Comparison: 10 LMWH vs UH (Sensitivity analysis)

Outcome: 2 PE

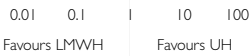
Study or subgroup	LMWH n/N	UH n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Geerts 1996	1/129	0/136		100.0 %	3.16 [0.13, 76.91]
Total (95% CI)	**129**	**136**		**100.0 %**	**3.16 [0.13, 76.91]**

Total events: 1 (LMWH), 0 (UH)

Heterogeneity: not applicable

Test for overall effect: Z = 0.71 (P = 0.48)

Test for subgroup differences: Not applicable



Analysis 10.3. Comparison 10 LMWH vs UH (Sensitivity analysis), Outcome 3 Mortality.

Review: Thromboprophylaxis for trauma patients

Comparison: 10 LMWH vs UH (Sensitivity analysis)

Outcome: 3 Mortality

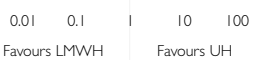
Study or subgroup	LMWH n/N	UH n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Geerts 1996	0/129	0/136		0.0 [0.0, 0.0]
Total (95% CI)	**129**	**136**		**0.0 [0.0, 0.0]**

Total events: 0 (LMWH), 0 (UH)

Heterogeneity: not applicable

Test for overall effect: Z = 0.0 (P < 0.00001)

Test for subgroup differences: Not applicable



Analysis 10.4. Comparison 10 LMWH vs UH (Sensitivity analysis), Outcome 4 Bleeding.

Review: Thromboprophylaxis for trauma patients

Comparison: 10 LMWH vs UH (Sensitivity analysis)

Outcome: 4 Bleeding

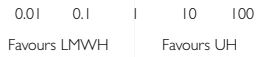
Study or subgroup	LMWH n/N	UH n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Geerts 1996	5/129	1/136		100.0 %	5.27 [0.62, 44.51]
Total (95% CI)	**129**	**136**		**100.0 %**	**5.27 [0.62, 44.51]**

Total events: 5 (LMWH), 1 (UH)

Heterogeneity: not applicable

Test for overall effect: Z = 1.53 (P = 0.13)

Test for subgroup differences: Not applicable



Analysis 10.5. Comparison 10 LMWH vs UH (Sensitivity analysis), Outcome 5 Major Bleeding.

Review: Thromboprophylaxis for trauma patients

Comparison: 10 LMWH vs UH (Sensitivity analysis)

Outcome: 5 Major Bleeding

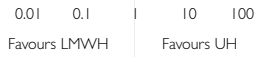
Study or subgroup	LMWH n/N	UH n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Geerts 1996	4/129	1/136		100.0 %	4.22 [0.48, 37.23]
Total (95% CI)	**129**	**136**		**100.0 %**	**4.22 [0.48, 37.23]**

Total events: 4 (LMWH), 1 (UH)

Heterogeneity: not applicable

Test for overall effect: Z = 1.30 (P = 0.20)

Test for subgroup differences: Not applicable



Analysis 10.6. Comparison 10 LMWH vs UH (Sensitivity analysis), Outcome 6 Minor Bleeding.

Review: Thromboprophylaxis for trauma patients

Comparison: 10 LMWH vs UH (Sensitivity analysis)

Outcome: 6 Minor Bleeding

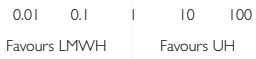
Study or subgroup	LMWH n/N	UH n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Geerts 1996	1/129	0/136		100.0 %	3.16 [0.13, 76.91]
Total (95% CI)	**129**	**136**		**100.0 %**	**3.16 [0.13, 76.91]**

Total events: 1 (LMWH), 0 (UH)

Heterogeneity: not applicable

Test for overall effect: Z = 0.71 (P = 0.48)

Test for subgroup differences: Not applicable



Analysis 11.1. Comparison 11 Pharmacological prophylaxis vs Mechanical prophylaxis (Sensitivity analysis), Outcome 1 DVT.

Review: Thromboprophylaxis for trauma patients

Comparison: 11 Pharmacological prophylaxis vs Mechanical prophylaxis (Sensitivity analysis)

Outcome: 1 DVT

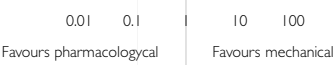
Study or subgroup	Pharmacological n/N	Mechanical n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Ginzburg 2003	1/218	6/224		100.0 %	0.17 [0.02, 1.41]
Total (95% CI)	**218**	**224**		**100.0 %**	**0.17 [0.02, 1.41]**

Total events: 1 (Pharmacological), 6 (Mechanical)

Heterogeneity: not applicable

Test for overall effect: Z = 1.64 (P = 0.10)

Test for subgroup differences: Not applicable



Analysis 11.2. Comparison 11 Pharmacological prophylaxis vs Mechanical prophylaxis (Sensitivity analysis), Outcome 2 PE.

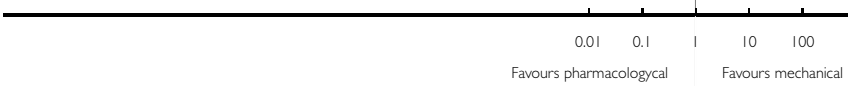
Review: Thromboprophylaxis for trauma patients

Comparison: 11 Pharmacological prophylaxis vs Mechanical prophylaxis (Sensitivity analysis)

Outcome: 2 PE

Study or subgroup	Pharmacological n/N	Mechanical n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Ginzburg 2003	1/218	1/224		100.0 %	1.03 [0.06, 16.32]
Total (95% CI)	**218**	**224**		**100.0 %**	**1.03 [0.06, 16.32]**

Total events: 1 (Pharmacological), 1 (Mechanical)
Heterogeneity: not applicable
Test for overall effect: Z = 0.02 (P = 0.98)
Test for subgroup differences: Not applicable



Analysis 11.3. Comparison 11 Pharmacological prophylaxis vs Mechanical prophylaxis (Sensitivity analysis), Outcome 3 Mortality.

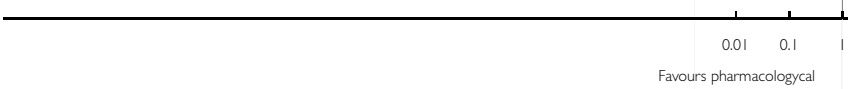
Review: Thromboprophylaxis for trauma patients

Comparison: 11 Pharmacological prophylaxis vs Mechanical prophylaxis (Sensitivity analysis)

Outcome: 3 Mortality

Study or subgroup	Pharmacological n/N	Mechanical n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Ginzburg 2003	0/218	0/224		0.0 [0.0, 0.0]
Total (95% CI)	**218**	**224**		**0.0 [0.0, 0.0]**

Total events: 0 (Pharmacological), 0 (Mechanical)
Heterogeneity: not applicable
Test for overall effect: Z = 0.0 (P < 0.00001)
Test for subgroup differences: Not applicable



Analysis 11.4. Comparison 11 Pharmacological prophylaxis vs Mechanical prophylaxis (Sensitivity analysis), Outcome 4 Bleeding.

Review: Thromboprophylaxis for trauma patients

Comparison: 11 Pharmacological prophylaxis vs Mechanical prophylaxis (Sensitivity analysis)

Outcome: 4 Bleeding

Study or subgroup	Pharmacological n/N	Mechanical n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Ginzburg 2003	13/218	8/224		100.0 %	1.67 [0.71, 3.95]
Total (95% CI)	**218**	**224**		**100.0 %**	**1.67 [0.71, 3.95]**
Total events: 13 (Pharmacological), 8 (Mechanical)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.17 (P = 0.24)					
Test for subgroup differences: Not applicable					

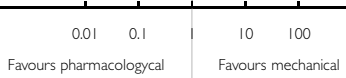
Analysis 11.5. Comparison 11 Pharmacological prophylaxis vs Mechanical prophylaxis (Sensitivity analysis), Outcome 5 Major bleeding.

Review: Thromboprophylaxis for trauma patients

Comparison: 11 Pharmacological prophylaxis vs Mechanical prophylaxis (Sensitivity analysis)

Outcome: 5 Major bleeding

Study or subgroup	Pharmacological n/N	Mechanical n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Ginzburg 2003	4/218	4/224		100.0 %	1.03 [0.26, 4.06]
Total (95% CI)	**218**	**224**		**100.0 %**	**1.03 [0.26, 4.06]**
Total events: 4 (Pharmacological), 4 (Mechanical)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.04 (P = 0.97)					
Test for subgroup differences: Not applicable					

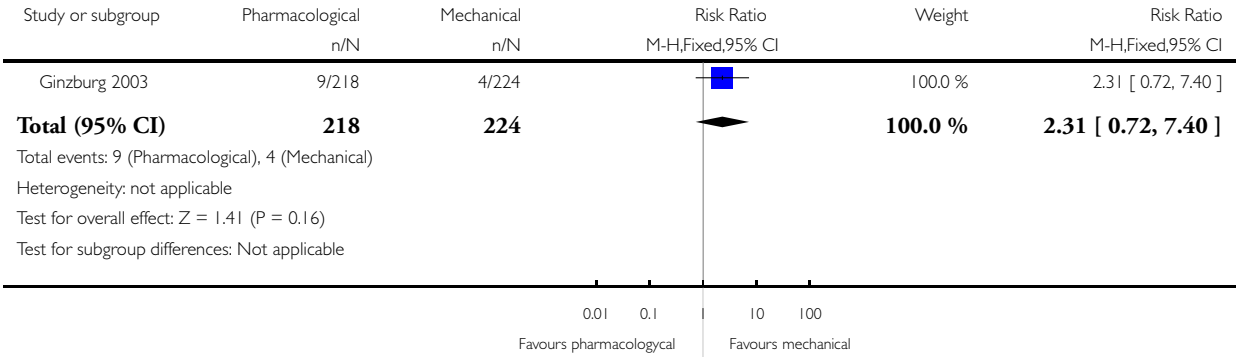


Analysis 11.6. Comparison 11 Pharmacological prophylaxis vs Mechanical prophylaxis (Sensitivity analysis), Outcome 6 Minor bleeding.

Review: Thromboprophylaxis for trauma patients

Comparison: 11 Pharmacological prophylaxis vs Mechanical prophylaxis (Sensitivity analysis)

Outcome: 6 Minor bleeding



APPENDICES

Appendix 1. Search strategy

Cochrane Injuries Group Specialised Register (searched April 30 2009)

1. (wound* or trauma* or injur* or fracture* or burn* or stab* or shot* or shoot* or lacerat* or accident*)
2. (thrombus* or thrombotic* or thrombolic* or thromboemboli* or thrombos* or thromboph*) or ((deep* and (vein* or ven*) and (thromb* or embol*)) or ((pulmonary or lung*) and (thromb* or embol*)) or (DVT or PE or VTE)
3. 1 and 2
4. Thromboprophylaxis or prophylactic* or prophylaxis or Heparin* or Anticoagulant* or Warfarin or Coumadin* or apo-warfarin or gen-warfarin or warfant or Coumadin or aldocumar or tedicumar or Antiplatelet* or anticoagulant* or Aspirin* or "acetylsalicylic acid" or acylpyrin or aloxiprimum or colfarit or dispril or easprin or ecotrin or endosprin or magnecyl or micristin or polopirin or polopiryna or solprin or solupsan or zorprin or acetysal or Pentassacharide* or fondaparinux or Heparin* or "vena cava filter" or "umbrella filter" anti-platelet*
5. 3 and 4

MEDLINE (Ovid) 1950 to April (Week 3) 2009

1. exp "Wounds and Injuries"/
2. (wound* or trauma* or injur* or fracture* or burn* or stab* or shot* or shoot* or lacerat* or accident*).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name]
3. 1 or 2
4. exp Venous Thromboembolism/
5. exp Venous Thrombosis/
6. exp Pulmonary embolism/

7. exp Thrombophlebitis/
8. (thrombus* or thrombotic* or thrombolic* or thromboemboli* or thrombos* or thromboph*).ab,ti.
9. (deep* adj3 (vein* or ven*) adj5 (thromb* or embol*)).ab,ti.
10. ((pulmonary or lung*) adj3 (thromb* or embol*)).ab,ti.
11. (DVT or PE or VTE).ab,ti.
12. 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11
13. (thromboprophylaxis or prophylactic* or prophylaxis).ab,ti.
14. exp Heparin/
15. exp Heparin, Low-Molecular-Weight/
16. exp Heparinoids/
17. exp Stockings, Compression/
18. exp Intermittent Pneumatic Compression Devices/
19. exp Stockings, Compression/
20. exp Anticoagulants/
21. exp Warfarin/
22. exp Platelet Aggregation Inhibitors/
23. exp Aspirin/
24. Heparin*.ab,ti.
25. ((compression or impulse or pneumatic or elastic*) adj3 (device* or stocking* or hose* or dressing* or bandage*)).ab,ti.
26. (Anticoagulant* or Warfarin or Coumadin* or apo-warfarin or gen-warfarin or warfant or Coumadin or aldocumar or tedicumar).ab,ti.
27. (Antiplatelet* or (platelet* adj3 aggregation adj3 inhibit*) or ((blood or platelet*) adj3 (antagonist* or antiaggrega*))).ab,ti.
28. (Aspirin* or acetylsalicylic acid or acylpyrin or aloxiprimum or colfarit or dispril or easprin or ecotrin or endosprin or magnecyl or micristin or polopirin or polopiryna or solprin or solupsan or zorprin or acetysal).ab,ti.
29. exp Vena Cava Filters/
30. ((vena adj3 cava adj3 filter*) or (umbrella adj3 filter*)).ab,ti.
31. (Pentassacharide* or fondaparinux).ab,ti.
32. or/13-31
33. randomi?ed.ab,ti.
34. randomized controlled trial.pt.
35. controlled clinical trial.pt.
36. placebo.ab.
37. clinical trials as topic.sh.
38. randomly.ab.
39. trial.ti.
40. 33 or 34 or 35 or 36 or 37 or 38 or 39
41. (animals not (humans and animals)).sh.
42. 40 not 41
43. 3 and 12 and 32 and 42

EMBASE (Ovid) 1980 to 2009 (Week 17)

1.exp Injury/
2.(wound* or trauma* or injur* or fracture* or burn* or stab* or shot* or shoot* or lacerat* or accident*).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name]
3.1 or 2
4.exp Vein Thrombosis/
5.exp Lung Embolism/
6.exp venous thromboembolism/
7.exp deep vein thrombosis/
8.exp Thrombophlebitis/
9.(thrombus* or thrombotic* or thrombolic* or thromboemboli* or thrombos* or thromboph*).ab,ti.
10.(deep* adj3 (vein* or ven*) adj5 (thromb* or embol*)).ab,ti.
11.(deep* adj3 (vein* or ven*) adj5 (thromb* or embol*)).ab,ti.

12.((pulmonary or lung*) adj3 (thromb* or embol*)).ab,ti.
13.(DVT or PE or VTE).ab,ti.
14.or/4-13
15.(thromboprophylaxis or prophylactic* or prophylaxis).ab,ti.
16.exp Heparin/
17.exp Low Molecular Weight Heparin/
18.exp Heparinoid/
19.exp compression garment/
20.exp Compression Bandage/
21.exp intermittent pneumatic compression device/
22.exp Vena Cava Filter/
23.exp Anticoagulant Agent/
24.exp Coumarin Anticoagulant/
25.exp Antithrombocytic Agent/
26.exp Acetylsalicylic Acid/
27.Heparin*.ab,ti.
28.(Anticoagulant* or Warfarin or Coumadin* or apo-warfarin or gen-warfarin or warfant or Coumadin or aldocumar or tedicumar).ab,ti.
29.(Antiplatelet* or (platelet* adj3 aggregation adj3 inhibit*) or ((blood or platelet*) adj3 (antagonist* or antiaggrega*))).ab,ti.
30.(Aspirin* or acetylsalicylic acid or acylpyrin or aloxiprimum or colfarit or dispril or easprin or ecotrin or endosprin or magnecyl or micristin or polopirin or polopiryna or solprin or solupsan or zorprin or acetysal).ab,ti.
31.((vena adj3 cava adj3 filter*) or (umbrella adj3 filter*)).ab,ti.
32.(Pentassacharide* or fondaparinux).ab,ti.
33.((compression or impulse or pneumatic or elastic*) adj3 (device* or stocking* or hose* or dressing* or bandage*)).ab,ti.
34.or/15-33
35.exp Randomized Controlled Trial/
36.exp controlled clinical trial/
37.randomi?ed.ab,ti.
38.placebo.ab.
39.*Clinical Trial/
40.randomly.ab.
41.trial.ti.
42.35 or 36 or 37 or 38 or 39 or 40 or 41
43.exp animal/ not (exp human/ and exp animal/)
44.42 not 43
45.34 and 3 and 44 and 14

CENTRAL (*The Cochrane Library 2009, Issue 2)*

#1 MeSH descriptor Venous Thromboembolism explode all trees
#2 MeSH descriptor Venous Thrombosis explode all trees
#3 MeSH descriptor Pulmonary Embolism explode all trees
#4 MeSH descriptor Thrombophlebitis explode all trees
#5 (thrombus* or thrombotic* or thrombolic* or thromboemboli* or thrombos* or thromboph*)
#6 ((deep*) near3 (vein* or ven*)) near5 (thromb* or embol*)
#7 (pulmonary or lung*) near3 (thromb* or embol*)
#8 DVT or PE or VTE
#9 (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8)
#10 thromboprophylaxis or prophylactic* or prophylaxis
#11 MeSH descriptor Heparin explode all trees
#12 MeSH descriptor Heparin, Low-Molecular-Weight explode all trees
#13 MeSH descriptor Heparinoids explode all trees
#14 MeSH descriptor Stockings, Compression explode all trees
#15 MeSH descriptor Intermittent Pneumatic Compression Devices explode all trees
#16 MeSH descriptor Stockings, Compression explode all trees

#17 MeSH descriptor Anticoagulants explode all trees
#18 MeSH descriptor Warfarin explode all trees
#19 MeSH descriptor Platelet Aggregation Inhibitors explode all trees
#20 MeSH descriptor Aspirin explode all trees
#21 Heparin*
#22 ((compression or impulse or pneumatic or elastic*) near3 (device* or stocking* or hose* or dressing* or bandage*))
#23 (Anticoagulant* or Warfarin or Coumadin* or apo-warfarin or gen-warfarin or warfant or Coumadin or aldocumar or tedicumar)
#24 Antiplatelet* or (platelet* near3 aggregation near3 inhibit*)
#25 (blood or platelet*) near3 (antagonist* or antiaggrega*)
#26 Aspirin* or acetylsalicylic acid or acylpyrin or aloxiprimum or colfarit or dispril or easprin or ecotrin or endosprin or magnecyl or micristin or polopirin or polopiryna or solprin or solupsan or zorprin or acetysal
#27 MeSH descriptor Vena Cava Filters explode all trees
#28 (vena near3 cava near3 filter*) or (umbrella near3 filter*)
#29 Pentassacharide* or fondaparinux
#30 (#10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29)
#31 (#9 AND #30)
#32 MeSH descriptor Wounds and Injuries explode all trees
#33 wound* or trauma* or injur* or fracture* or burn* or stab* or shot* or shoot* or lacerat* or accident*
#34 (#32 OR #33)
#35 (#31 AND #34)

ISI Web of Science: Science Citation Index Expanded (SCI-EXPANDED) (1970 to April 2009),
ISI Web of Science: Conference Proceedings Citation Index-Science (CPCI-S) (1990 to April 2009)

#1 Topic=(wound* or trauma* or injur* or fracture* or burn* or stab* or shot* or shoot* or lacerat* or accident*)
#2 Topic=(thrombus* or thrombotic* or thrombolic* or thromboemboli* or thrombos* or thromboph*) OR Topic=(deep* same (vein* or ven*) same (thromb* or embol*)) OR Topic=((pulmonary or lung*) same (thromb* or embol*)) OR Topic=(DVT or PE or VTE)
#3 #1 and #2
#4 Topic=(thromboprophylaxis or prophylactic* or prophylaxis or Heparin* or Anticoagulant* or Warfarin or Coumadin* or apo-warfarin or gen-warfarin or warfant or Coumadin or aldocumar or tedicumar or Antiplatelet* or Aspirin* or acetylsalicylic acid or acylpyrin or aloxiprimum or colfarit or dispril or easprin or ecotrin or endosprin or magnecyl or micristin or polopirin or polopiryna or solprin or solupsan or zorprin or acetysal or Pentassacharide* or fondaparinux)
#5 Topic=(platelet* same aggregation same inhibit*) OR Topic=((blood or platelet*) same (antagonist* or antiaggrega*)) OR Topic=((compression or impulse or pneumatic or elastic*) same (device* or stocking* or hose* or dressing* or bandage*)) OR Topic=(vena same cava same filter*) OR Topic=(umbrella same filter*)
#6 #4 or #5
#7 #3 and #6
#8 Topic=(((singl* OR doubl* OR trebl* OR tripl*) SAME (blind* OR mask*))) OR Topic=(randomised OR randomized OR randomly OR random order OR random sequence OR random allocation OR randomly allocated OR at random OR randomized controlled trial) OR Topic=(controlled clinical trial OR controlled trial OR clinical trial OR placebo) AND Topic=(human*)
#9 #7 and #8

PubMed [http://www.ncbi.nlm.nih.gov/sites/entrez] (searched 29 April 2009: limited to: added to PubMed in the Last 180 days)

#1 wound* OR trauma OR traumatic OR traumas OR traumatolog* OR injur* OR fracture* OR burn* OR stab OR stabbing* OR stabbed OR stabwound* OR stabs OR shot* OR shoot* OR lacerat* OR accident*
#2 thrombus* OR thrombotic* OR thrombolic* OR thromboemboli* OR thrombos* OR thromboph*
#3 DVT OR PE OR VTE
#4 deep* AND (vein* OR venous) AND (thrombos OR thromboe* OR emboli*)
#5 #2 OR #3 OR #4
#6 (thromboprophylaxis OR prophylactic* OR prophylaxis OR Heparin* OR Anticoagulant* OR Warfarin OR Coumadin* OR apo-warfarin OR gen-warfarin OR warfant OR Coumadin OR aldocumar OR tedicumar OR Antiplatelet* OR Aspirin* OR acetylsalicylic acid OR acylpyrin OR aloxiprimum OR colfarit OR dispril OR easprin OR ecotrin OR endosprin OR magnecyl OR micristin OR polopirin OR polopiryna OR solprin OR solupsan OR zorprin OR acetysal OR Pentassacharide* OR fondaparinux
#7 platelet* AND aggregation AND inhibitor*

#8 (blood or platelet*) AND (antagonist* or antiaggrega*)
#9 (compression OR impulse OR pneumatic OR elastic*) AND (device* OR stocking* OR hose* OR dressing* OR bandage*)
#10 (vena AND cava AND filter*) OR (umbrella AND filter*)
#11 #6 OR #7 OR #8 OR #9 OR #10
#12 #1 AND #5 AND #11
#13 ((randomized controlled trial[pt] OR controlled clinical trial[pt]) OR (randomized OR randomised OR randomly OR placebo[tiab]) OR (trial[ti]) OR ("Clinical Trials as Topic"[MeSH Major Topic])) NOT (("Animals"[Mesh]) NOT ("Humans"[Mesh] AND "Animals"[Mesh]))
#14 #12 AND #13

CONTRIBUTIONS OF AUTHORS

All authors contributed to this manuscript.

DECLARATIONS OF INTEREST

None known.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

On the advice of the Cochrane Injuries Group's editors we have specified mortality as the primary outcome of the review. DVT and PE are listed as secondary outcomes.